FUNDAMENTALS OF PATHOLOGY

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OF

PATHOLOGY

FOR STUDENTS AND GENERAL PRACTITIONERS OF MEDICINE AND DENTISTRY AND FOR NURSES IN TRAINING SCHOOLS

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EIGHTY-ONE ILLUSTRATIONS, INCLUDING ONE COLOR PLATE

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PREFACE

This volume makes no pretense of being either complete or perfect. All that it pretends to do is to make it possible for certain groups of students of one or another aspect of medicine to get a bird's-eye view of the problems of pathology, and of the methods of disease.

There is a rapidly growing need among the students of dentistry for something more than the often superficial and somewhat disconnected accounts of the basic principles of their art. More and more the dentist is realizing that his problems and those of the physician are very close together; so close that it seems that dentistry will no longer be looked upon as essentially separate from medicine and surgery. There is, then, every reason why the dentist should be provided with a systematic treatise, which, while it is not applied specifically to his work, will form a basis for closer relationships with his fellow students in medicine.

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FUNDAMENTALS OF PATHOLOGY

CHAPTER I.

INTRODUCTION.

It is of course realized that the body is a composite organism, i. e., that it is composed of organs, and that the organs are composed of cells. It follows from this that the various functions of the body depend upon the activities of the cells. As Guyer has expressed it, "Every biological manifestation of function and process from the flow of thought to the pathology of cancer resolves itself in last analysis into a problem of the living cell." It is exactly the same with us whether we deal with a single cell like a bacterium or an ameba, an organ like the liver or the whole human body, with this exception,—that in the first cases we deal with single cells which constitute the whole organism, while in the latter cases we deal with groups of cells—cells which act together in harmony.

Even in the smallest of the unicellular organisms the cell body is not homogeneous but shows certain structures which are known as primitive organs. In some cases we recognize only a nucleus; sometimes not even that. In other cases, we find other things than the nucleus, for instance, a contracting vacuole, which is an excretory organ. These organs are parts of the cell body which have been differentiated from the rest of the protoplasm and set apart to do certain specific things. The cytoplasm, for instance, may be largely responsible for the ingestion and assimilation of food, while the

nucleus has rather to do with functions of reproduction and growth.

These primitive organs therefore play a part in the lower organisms which the more complex organs play in the human. They are parts of the living organism which perform certain tasks which no other part can do so well, and often cannot do at all. They are not, however, independent of the body as a whole but are carefully coordinated in the organism and depend for their activities upon one another. Remove the nucleus from a cell and that cell no longer grows. Remove the liver from the man and he dies. In the lower organisms the correlation is relatively simple. In the higher forms of life it becomes more and more complicated as the conditions of life become more and more complex.

So long as the coordination remains relatively undisturbed, i. e., not affected beyond certain limits, health results. When these limits are passed, disease is produced. Health then depends upon cellular and organic coordination; disease upon lack of coordination.

In the lower forms of life, as in the ameba, the correlation between different parts of each cell is the important thing. In more advanced forms, it exists between cells. In the still higher forms, groups of cells are involved. Such groups of cells may form large organs as, for instance, the liver, or pancreas, or, on the other hand, may be merely a part of an anatomical organ as illustrated in the medulla of the adrenal or the cells of the respiratory center.

The cells of the body are composed, we are told, of protoplasm. The protoplasm is divided according to its varying chemical structure into cytoplasm and nuclear material. Both are albuminous in constitution. Besides these substances there are others which also are present in all cells; for instance, fats, lipoids (such as cholesterin and lecithin), glycogen; and still others which are

present in only certain types of cells, such as keratin in epithelial cells, pigments in some epithelial cells, in the retina cells, in certain nerve cells and their derivatives, and in the corpus luteum of the ovary. The bodies which are present in all cells are spoken of as primary constituents; those present only in certain types of cells, as secondary constituents. It is the latter which often help us in deciding what type of cells we are dealing

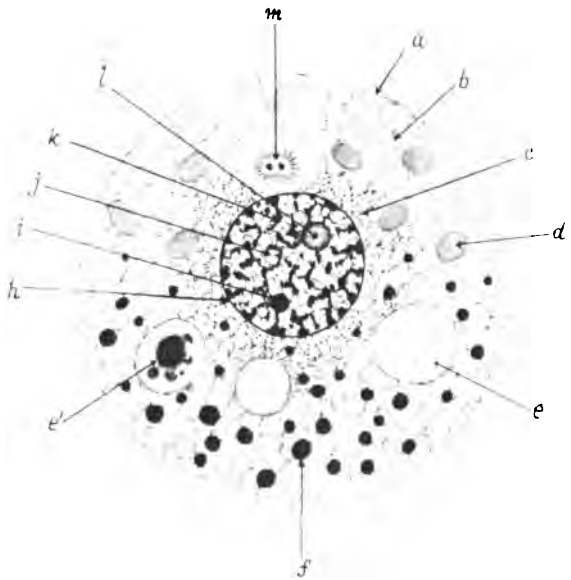

Fig. 1. Diagrammatic representation of cell structure. *a*, Cell-wall or membrane; *b*, Cytoreticulum, or spongioplasm, containing the hyaloplasm in its meshes; *c*, Endoplasm; *d*, Plastids or protoplasts; *e*, "Vacuole;" *f*, Digestive "Vacuole," containing partially digested cell inclusion; *g*, Metaplasm (granules of pigment, ingested food, etc.); *h*, Nuclear membrane; *i*, "Net-knot" or karyosome; *j*, *k*, Nuclear network, consisting of chromatin and linin, and enclosing in its meshes the nuclear hyaloplasm or karyolymph; *l*, Nucleolus or plasmosome; *m*, Astral system, containing divided centrosome. (After Wilson, from Beattie and Dickson.)

with and perhaps whether or not, if we know the type of cell, what abnormal process is affecting the cells. The presence of a certain substance (melanin) in cells when no melanin is present under normal conditions, is evidence of a pathologic process. The same thing may be

said of enzymes. The presence of pepsin in the kidney would be just as abnormal as the absence of it in the stomach. It is interesting to know that the secondary constituents depend upon the activities of the primary ones.

One of the most important constituents of all protoplasm is water. Were it not for this substance, life could not exist, for without it solutions of food substances and salts could not be made in the body,—and the cells all depend upon solutions for their nourishment. In the gastrointestinal tract the foodstuffs are changed by means of ferments from insoluble states to soluble ones. Albumins become changed into peptones and amino-acids and these absorbed into the tissues, are again built up into relatively insoluble combinations. And it is mainly nitrogenous substances (proteins), the carbohydrates (sugars), and the fats, which serve as foods. For them the water is a vehicle of transmission from one part of the body to another. The salts, on the other hand, probably have no nutritive value, but are effective in modifying the protoplasm so that it has greater affinity for water in which the nutritive substances are dissolved. Protoplasm is a substance which belongs to the same physical category as glue, and gelatine, i. e., it is a colloid,—a nitrogenous colloid. When a salt in solution comes in contact with a colloid of the type of protoplasm, the colloid gives up water. When it comes in contact with an acid is takes up water.

In the body, the tissues are normally neutral. But whenever they are active they tend to be split up into simpler chemical substances which invariably are acid in character. Under these circumstances the cells absorb water with its dissolved substances, foodstuffs and salts. When the concentration of salts reaches a certain point, water absorption ceases. When it passes that point, water and dissolved substances are given up by

the protoplasm (excretion), and since the blood serum is always, though very little, more acid than the tissues, because of the presence of acid excretions (carbonic acid and other substances), the tendency is for substances in solution to continually pass out of the cells into the serum. At the same time actively functionating cells constantly produce acids and so there is the constant tendency for cells to take up water and dissolved substances. It is therefore upon local variations in acidity and alkalinity that absorption and secretion depend.

So pathology while it is, as the word signifies, the study of disease, it is also fundamentally a study of the physics and chemistry of the body colloids, particularly the nitrogenous colloids. We shall, however, in the following chapters not make a fundamental study of the facts of disease, but will devote ourselves to a more superficial view of the problems of disease.

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PART I—GENERAL PATHOLOGY

CHAPTER II.

HEALTH AND DISEASE.

As we have said, health depends upon coordination of cellular processes: disease depends upon a lack of such coordination. If we accept this conception then we see that health and disease depend upon two things; the structure of the cells of the body and the reaction of them to influences without the cells.

Were the cells constant in structure and were the environment constant, then cellular disease would not exist. Were the body constructed in a constant fashion, and were the surroundings of the body constant, then disease of the body would not exist. So disease of the body depends upon (1) the structure of the body and (2) the environment.

We may illustrate this in the following ways:

1. Suppose we consider a normal human being. His digestion is perfect. His temperature is normal. He is happy and contented, and is free from any annoyance, however petty. Suppose he take by mistake a solution of bichloride of mercury, thinking it water. Suppose in place of the corrosive sublimate, the water contains typhoid bacilli, or cholera spirilla. Suppose he is struck by a falling object. In either case damage to the body results. He is poisoned, we say in the first case. He becomes infected, in the second. He receives a trauma, in the third. He is upset. No longer are the functions of the body carried out in a normal fashion. His peace

of mind is lost. He is sick. He serves us as an example of an organism, internally perfect, to start with, which has suffered from abnormal conditions in the environment.

II. Suppose, again, we take a case in which the surroundings of the individual are almost perfect—let us make them perfect. Let us say that the water supply is absolutely clean, the food supply fresh, the cuisine unexcelled, the surroundings normally sterile. And yet the individual whom we are considering does not behave in a normal fashion. Perhaps he has some "nervous" condition; perhaps he passes too much sugar in his urine; perhaps he reacts toward stimuli which come from his surroundings in a totally strange manner. He weeps at small things; he raves at objects; he has maniacal attacks; perhaps he is depressed. He does not easily withstand changes of temperature. Evidently something is the matter inside the body. The cells do not respond to stimuli as they should. He is phlegmatic we say, or he shows spleen, he has a bad disposition, or a weak constitution. Here we have an example of the effect of a normal environment on a body which is constructed badly.

III. Suppose still again, we consider an individual who because of improper care has become run down, we say,—anemic, tired, worn out. He has allowed a perfectly good environment to play havoc with his body. The internal arrangements have been damaged so that while others in the same environment preserve their health, he becomes tuberculous, let us say. Because he is "run down" he becomes infected. He is careless of chill and fatigue and "takes" pneumonia. He allows his tonsils or teeth to get into a bad state of repair, and develops rheumatism and its attendant states. He is allowed or forced by parents or society to think and feel and behave in wrong directions and, following false gods,

he becomes a criminal. Here we have had under consideration the results to be expected from combinations of internal abnormalities together with bad surroundings.

There are then three points—categories into which we may classify disease:

I. Those in which there is a primary external abnormality.

II. Those in which there is a primary internal abnormality.

III. Those in which both internal and external abnormalities play a part.

Sometimes we say that a disease, or a tendency is inherited or congenital. What do we mean by that? An inherited disease is one which appears in similar form in several generations of individuals of the same family. A congenital disease is one which appears at birth. Such a disease may be therefore also inherited.

Inherited diseases are the evidence of some permanent variation of the cellular correlations of the body, and being permanent the variation tends to reappear in succeeding generations. A congenital disease is, on the other hand, oftentimes a temporary variation, or an isolated example of disease appearing at birth. Perhaps we should be safe in saying that a congenital abnormality is one which is acquired during the intrauterine period of life, while inherited is applied to conditions which depend upon permanent changes in the germinal plasm.

Suppose we illustrate this in the following ways:

I. Take an individual who after birth exhibits certain abnormalities which were characteristics of his father, and of his grandfather, and great grandfather. We would say that he was the subject of an inherited condition. Take an example such as color-blindness which is transmitted from generation to generation, chiefly in

the men of a family, or hemophilia, a condition which characterizes "bleeders." Evidently in these cases the fundamental qualities of the germinal protoplasm have suffered a change.

II. On the other hand, take the case of an apparently healthy mother who, just previous to conception, or after conception, while the fetus is developing in the uterus, becomes intoxicated, let us say with alcohol (alcohol is perhaps the best example we can choose). The germinal plasm (the ovum) or the embryo (fetus) is affected by the poison so that after it is born it shows or develops abnormalities which are completely foreign in the family of mother or father. The child is the subject of a congenital condition or perhaps disease. It is apt to be less stable mentally ("neurotic") than an otherwise normal child. Its general mental condition is apt to be below the normal average (deficient), or it may be far below the average (idiocy, feeble-mindedness). If such a child reaches maturity it may become an alcoholic, and then certain persons speak of it as having an "hereditary craving" for alcohol, whereas it is merely *congenitally* mentally unstable. If, again, such a child reaches maturity, and has children and those children are also mentally unstable, then we may say that they show an hereditary taint, or hereditary mental instability.

Perhaps a mother, during the period of gestation, becomes infected with one or another disease. If the child at birth has the same disease, that disease is congenital, not inherited. The infectious diseases are not hereditary, whether we speak of syphilis, gonorrhea, tuberculosis, or measles. On the other hand, diseases of the mother which do not directly affect the child in utero may produce immunity to the maternal diseases, and so we have congenital immunity to disease. If the conditions which produce immunity affect permanently the germinal tissues, hereditary immunity may result.

CHAPTER III.

THE CAUSES OF DISEASE.

Regardless of whether the basis of disease rests on intrinsic or extrinsic variations, we can divide the causes into four great groups; namely, physical, physico-chemical, chemical, sociologic. These we will discuss in the order in which they have been named. This classification is of course arbitrary, and is made for convenience sake, for, with few exceptions, all injuries produce chemical damage within the body. That is to say, they lead to internal disorders of a chemical nature in the absence of which they would be of little or no importance, so far as the life or death of the whole organism is concerned. A cut or a bruise is of relatively small importance unless infection occurs or severe hemorrhage takes place. In the first instance, the tissues are prepared for the growth of bacteria; in the second, the tissues do not receive an adequate supply of oxygen because the oxygen carrying material of the blood has been lost.

It is of course evident that the mechanical and physical causes of disease are very commonly primary, but it is the secondary effects which are of greatest significance. The symptoms of disease following mechanical or physical insults are the expressions (for the most part) of these secondary effects. Both pressure and tension act in producing variations in the nutritive activities of cells, and no matter whether these forces are exerted upon normal or abnormal cells, tissues or organs, changes are inaugurated which express themselves in various directions, such as hypertrophy, atrophy, degenerations, or necrosis (of which more later), which are

the results of interference with nutritive (chemical) activities.

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Physical Causes.

The physical causes, as we shall group them, are predominantly mechanical ones, and their effects are spoken of as traumas (or traumata). In this group are (1) pressure, (2) tension (or strain), and (3) combinations of pressure and tension.

It must be evident to everyone, even if he has only a butcher-shop acquaintance with anatomy, that pressure is an important factor in producing the characteristic form of organs. One need only mention the lungs, the brain, the liver, to call attention to this factor. Were it not for the pressure exerted upon solid organs they would probably all be round. This is illustrated in the case of accessory spleens and livers which are not firmly attached, but hang more or less loosely in the body cavity and which are always round, quite unlike the larger fixed organs. The markings (grooves) on the surfaces of bones made by blood vessels, the very surfaces themselves, are examples of similar effects of normal pressures on normal organs.

In the category of phenomena resulting from abnormal pressures on normal organs, there are many everyday illustrations. Among them are corns, calluses, ingrowing toe nails. In former times, the days of tight lacing, the weird corset-liver was not infrequent. More important than these changes in form, are the symptoms produced by pressures, symptoms which indicate interference with function. In this connection one recalls

the "going-to-sleep" (anesthesia) of a foot from pressure upon a nerve trunk; the headache caused by a too tight collar; the bed-sores (decubitus) and "pressure spots" on the backs of bed-ridden patients; the swelling of the feet and appearance of varicose veins from tight garters. Also, in this group belong the erosions of bone caused by the intermittent pressure of aneurisms, the blistering of the hands by unusual manual work; the smothering (asphyxia) brought about by the pressure of tumors on the trachea; the difficulty in swallowing (dysphagia) caused by pressure upon the esophagus, and, an extremely frequent occurrence, the appearance of hemorrhoids (piles) from internal pressure in the bowels (constipation).

When normal or abnormal pressures act upon abnormal organs, the consequences are often still more severe. In this group we note the curvatures,—exemplified in knock-knees and bow-legs,—in rickets, as well as the spontaneous fractures of bones which have been affected by primary diseases of the bone. In these the bones are so weakened that even normal pressures warp and bend them and even cause them completely to give way.

Internal pressures (distention) also produce, not merely changes of form but also, symptoms. A too great quantity of blood within the heart embarrasses it. An accumulation of fluid in the ventricles of the brain causes a gradual disappearance (atrophy) of the brain substance, caught as it is between the fluid and the bony skull.

The effects of pressures depend largely upon the duration and continuity of action. Continuous pressure of moderate or extreme intensity may produce death (necrosis) of tissue while one of great intensity, acting intermittently, may produce only growth of tissue (hypertrophy) as in calluses. Obviously the continuous pressures are of most serious import.

It must be apparent that the place of action of a physical force and the character of the agent must be important items in considering the effects of a trauma. An incision made with a clean sharp knife may be of no more than very transient importance and may have no appreciable effect upon the economy provided it does not open a large vessel or injure a vital organ. A laceration produced by a dull dirty knife is more serious. A clean punctured wound may do no essential damage or it may cause death. A black eye (contusion) is rarely of importance, while a lacerated contusion is more immediately serious and potentially dangerous. A concussion may be either temporarily or permanently evil, depending upon the degree of force and the condition of the organs which are affected.

All these types of damage (traumas) produce tissue destruction. Disorganized tissue is an excellent culture medium, and so, since bacteria are constantly present on and in the skin, and frequently in the blood, traumas tend to be complicated by infections. Moreover traumas may lead to dislocations of cells, and such cells growing and reproducing in abnormal positions may produce tumors.

Tension produces frequent disorders, some of them of considerable significance, some of them rarely even recognized. Physiologically strain is the important cause of strengthening of the fibrous unions of muscle and bone. It accounts in a large measure for the presence of the tuberosities and other points of attachments of muscles. How it does this, is not definitely understood, but it is possible that the stretching of the tissues acts as a stimulus to the cells and so they make better use of the normal supply of food, or that intermittent application of the force increases the supply of food (blood) carried to the cells, much as happens during massage.

The effects of severe strain are well known in sprains of various sorts, as well as in the less severe strains. In the latter the tendons or their attachments are but moderately damaged. In the former they are often ruptured. In the case of muscular strain, whether of the skeletal muscles or of the eye muscles—for instance, eye-strain, fatigue is produced, with subsequent loss of power, and even atrophy or wasting.

Physico-Chemical Causes.

In this group we deal with such influences as atmospheric pressure, electricity, x-rays, radium, light and light waves, heat and cold, all of which are physical agents which produce both physical and chemical changes in the body, but of which the chemical effects are most important. They form a boundary group of influences standing between the more purely physical and the more purely chemical. In some instances the distinction is very little evident. For instance, the effects of sudden changes of atmospheric pressure such as occur in caisson disease are quite different from those of the gradual changes which occur when a person goes from one altitude to another. In the first instance, the blood absorbs more than a normal amount of atmospheric gases (oxygen and nitrogen chiefly), and this, when the pressure is suddenly removed, is set free in the blood and the bubbles of gas plug the small blood vessels. The phenomenon is quite similar to that observed in uncorking a soda water bottle. In the latter case, the decreased pressure apparently acts as a stimulant to the blood producing organs, and this results in a large number of blood cells.

Electric currents act upon the tissues of the body much as they do upon materials in a test tube. A current passed through a solution is modified so that certain particles pass to one pole while others pass to the other

(ions; electrolytic dissociation). In the body a similar process occurs only it is more complex. When such dissociation affects intensively such parts of the body as the respiratory center, death is immediate.

The method of action of the x-rays and radium we do not understand. Depending, however, upon the time of exposure, or the intensity of the rays, perhaps also upon the quality of the rays (the proportion of alpha, beta and gamma rays) cells may either be destroyed and so produce x-ray or radium burns, or may undergo hypertrophy, and ultimately give rise to x-ray cancers.

Light rays are antagonistic to life if they are sufficiently concentrated. Even diffused light is harmful to some forms of life. This is especially true of certain of the lower forms of life, particularly of the bacteria. It is not true of man.

Light is undoubtedly a stimulus to the chemical activities of cells, just as it accelerates many chemical reactions outside the body (silver salts in photography), and it may be true that light is more destructive to the bacteria because it is able more readily and thoroughly to penetrate their bodies and so start processes which result in self-destruction. In the large organisms, such as man, growth is favored by light. Metabolism is abnormally slow in darkness. Children of the light are physically larger than "basement children." These effects are in part due to the heat producing rays (red and infra-red); in part to the stimulant rays (violet and ultra-violet).

We know better the effects of the heat producing rays. We know the reddening of the skin with the subsequent soreness and blistering (vesiculation, sunburn), and the also subsequent increase of pigment in the skin (pigmentation, tanning). We also know the condition called sunstroke (insolation). Sunstroke is a condition which is caused indirectly by the action of the red and infra-

red (heat) waves of light. It is the result of insufficient elimination of heat from the body. When the body retains its heat, the chemical processes within it are accelerated, exactly as the chemical processes in a test tube mixture are hastened by waving over the flame. The result of this is that poisonous products of metabolism are more rapidly produced than at normal temperature, too rapidly to be excreted,—and the body suffers. If the heat of the body is not so extreme and if its action is spread out over a longer time, the organism loses water, by perspiration, in abnormal amount, and so the main solvent of the substances in the body is lost to an extent that the poisonous products of metabolism accumulate. This produces heat exhaustion.

Heat produces the effects which are generally known as burns. In the case of a slight burn (burn of the first degree) the skin is reddened, swells, and is painful. If the burn is slight and the action continued for some time, the skin is apt to become pigmented as in sunburn. If the burn is of a more severe character, the skin is not merely reddened, swollen and painful, but shows the presence of blisters, large or small (burns of the second degree). If the burn is still more severe the whole thickness of the skin may be affected. It is killed (undergoes necrosis) by the heat; the protoplasm of the cells and of the blood is coagulated, and the dead tissue sloughs away and leaves ulcers (burns of the third degree). In still more severe cases the skin is charred (carbonized) and we speak of burns of the fourth degree.

The effects of burns upon the whole organism depend upon the extreme pain, the absorption of dead materials from the skin, the infection of the burned areas, and the formation of disfiguring scars.

The effects of cold are, in some respects similar to those caused by heat. That is to say, cold may produce death of tissues by blocking the blood vessels. In se-

vere cases this is brought about by rapid thawing of the frozen tissue. In the course of freezing the water of the tissue solidifies in crystalline form, in other words, it is partially separated from the rest of the constituents. During rapid thawing the water is set free and not enough time is given it to reunite with the other substances. The result is blocking of the blood vessels and death of tissue.

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Chemical Causes.

The body may be affected by the most various substances, some of which produce very apparent gross effects, as, for instance, sulphuric acid, caustics of various sorts; some of which produce no obvious gross effect, as, for instance, poisonous gases, and the toxins produced by bacteria. These substances poison the body, some of them locally, some of them generally (intoxication). Many of them are products of living organisms, such as bacteria (bacterial toxins), many the product of unorganized chemical action (the caustics, acids, organic and inorganic poisons), and some of them are the products of the body itself. The fact that some are produced by the body while some are produced outside of it, allows us to classify them as *exogenous* and *endogenous,* while the fact that some are the products of living bodies, chiefly parasites, allows us to group them also as *parasitic* and *non-parasitic.* We make, therefore, the following schema:

A. Intoxications of exogenous and non-parasitic origin.

B. Intoxications of exogenous and parasitic origin (infections).

C. Intoxications of exogenous and saprophytic origin (meat poisonings, etc.).

D. Intoxications of endogenous and non-parasitic origin.

In the first group which concerns itself with exogenous and non-parasitic intoxications, belong the effects produced by the chemical substances,—strong acids, mineral or organic, silver nitrate, carbolic acid and the like. These as a rule act by killing the cells (coagulating their protoplasm) upon which they act. Sometimes, however, the local action is less important than the general action, or the action in other organs, than the one upon which the substance acted primarily. This is true of certain gases, for instance hydrocyanic acid gas, which, breathed into the lungs, causes death by its action upon the central nervous system. Carbolic acid likewise, if introduced into the body in dilute solutions, does less damage in the gastrointestinal tract than in the kidneys. Examples could be multiplied, and may be found in any pharmacology. Alcohol is the most useful example perhaps, because of its local, general and social effects. It may be useful to call to mind the so-called selective action of poisonous substances, illustrated by strychnine which affects the spinal cord; carbon dioxide which affects the respiratory center; and barium chloride which affects the muscle of the blood vessels.

The second group, that in which the exogenous parasitic intoxications belong, is concerned mainly with matters which are studied in bacteriology. They comprise the infections, which, though in certain cases the symptoms are due to the presence of the parasites themselves, are as a rule the result of the chemical action of the substances elaborated by the bacteria (see p. 41).

The exogenous saprophytic intoxications are ones caused by what are ordinarily called non-pathogenic organisms. They are the result of poisoning with substances produced by the microorganisms during splitting up of food materials. Such substances are the various amines, formed from proteins during putrefaction. A connecting link between this group and the previous ones

are the gastrointestinal intoxications or toxemias, often erroneously called autointoxications (see p. 149).

The last group comprises a series of metabolic disturbances which are coming to be of greater and greater significance, namely, the disturbances which result from imperfect correlation of function of physiologically associated organs, chiefly those called the glands of internal secretion, or the ductless glands (see p. 53).

Infection.

By infection we mean the entrance of living organisms (bacteria, protozoa, metazoa) into the bodies of other animals. In certain instances, the penetrating organisms are confined to the skin (acarus, itch mites) where they live and cause disturbances which are largely irritations, and which are not followed by the general reaction called immunity. In other cases organisms (intestinal worms) enter the gastrointestinal tract where they live and cause disturbances which are, in part, irritative, in part, toxic. Evidence of the toxic effects are given by changes in the structure of the blood (eosinophilia, etc.). In still another group of cases, the parasites penetrate into the tissues (bacteria, metazoa) where they reproduce and by their toxins give rise to local and general effects, which in some instances are so characteristic that we speak of definite disease. In some such cases the growth of the parasites in the body is followed by immunity (bacterial diseases, infectious diseases), in others, it is not (infections with such parasites as tapeworms, trichina, filaria, etc.).

Bacteria enter the body constantly, even during health. They also enter the tissues to which they are carried from the intestinal tract or infected tonsils or teeth, sometimes by leucocytes which have engulfed them, sometimes by their own activities. As a rule (in health) they are destroyed. When they succeed in living and multiplying

they cause infectious diseases, the symtoms of which may be due to mechanical effects, such as plugging of vessels, to toxic (chemical) effects or to both.

Normally, that is, in the state of health, the body can withstand the attacks of its bacterial foes, but a damaged body is not so resistant. For instance, it is well known that bacteria are commonly present, not only on the skin, but in it and yet these bacteria do but little damage. But after a cut or a bruise, "festering" is quite common. Often this is due to bacteria introduced during the cutting. Often it is due to the bacteria of the skin which are able to grow in damaged tissue. "Stitch abscesses" arise in the same way. A person with a normally acid gastric juice is infected with difficulty with cholera. But let him neutralize the acid juice with alkali and then he becomes very susceptible. In many conditions (for example, after using alcohol) the gastric contents are neutral or alkaline.

But beside such things, the resistance of the body depends upon many other factors, such as species, age, physical condition, nutritive conditions, on the one hand, and upon the virulence of the bacteria on the other. In brief, infection is determined by the relative virulence of the infecting organisms.

What is often called predisposition to infection is a real enough thing provided we use the term broadly. "Predisposition to tuberculosis" is however not a valuable phrase. An individual who is little resistant to infection is prone to acquire the frequent diseases, i. e., those from which many of his fellow beings are infected. The opportunities for infection with tuberculosis are legion. "Predisposition to tuberculosis" then is no more than a lack of resistance on the part of the individual to many infections, coupled with multiplied *exposition* to tuberculosis. The factor of exposition is probably the important one in the notable incidence of certain diseases in

children at the time when they begin to creep and to be handed from relative to relative. They begin to be exposed more systematically to infection. In creeping they soil their hands, and every object of interest is carried to the mouth for experimentation. They are kissed by every chance acquaintance. Tuberculosis is frequent in children in the early years of life.

Susceptibility to infection is another matter, and depends upon presence or absence of immunity and upon the relative resistance of the body, which latter may be lowered by various effects, such as fatigue, hunger, cold, intoxications (especially alcohol), by previous infections, and by secondary simultaneous infections.

Immunity results from the ability of the cells of the body to chemically fix or modify toxic substances which are brought to them by the blood, and is a quality which is sometimes inherited. It may also be the result of the inability of the cells of the body to make any use whatever of the toxins.

The effects of fatigue, hunger and cold are frequently seen in cases of "taking cold" [nasal infections (coryza); pneumonia].

The effects of intoxications we have already called attention to in speaking of alcohol and cholera.

The effects of previous infections are seen in cases, which, having had measles, develop tuberculosis or pneumonia: of simultaneous infection as to the appearance of tuberculosis during whooping cough.

Local infections produce local inflammation (boils, abscesses, furunculosis). General infections (bacteremia, septicemia) produce general effects, such as various types of tissue degenerations, fever, and other disorders of metabolism which are grouped under the term, the *effects* of *intoxications*.

Certain infective agents remain localized and produce general effects by means of soluble toxins (diphtheria,

tetanus) which effects we refer to toxemia as opposed to septicemia.

Sometimes bacteria localized at first, enter the blood stream and form new foci of growth as in furunculosis. This process of distribution from a primary focus we call metastasis: the condition is often called pyemia, or septicopyemia.

In latent infections, the bacteria remain in an inactive state in the tissues (tuberculosis).

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Sociologic Causes of Disease.

Very possibly it will seem strange and out of place in a volume of this sort to even mention social surroundings as a factor in disease. Nevertheless there is very probably no more important aspect of disease than the social. The character of associates, parents, and relatives; the formation of habits because of special associations; the growth of imitations of other individuals; the character of instruction in educational institutions; and the possibility of permanence of early impressions received in the juvenile or even in the infantile period of life,—all are entirely worthy of the attention they are only beginning to receive. It is in this field that the application of experimental psychology is beginning to prove of the utmost value, and it is here that medicine appears as a territory standing between sociology and normal psychology. In this field the benefits of preventive medicine will, in the future, be as striking and as valuable as they have shown themselves to be in the better known and perhaps more obvious fields of hygiene.

It will perhaps be discovered that what we call hereditary, in certain and very frequent instances, is not that, but is in reality social in a broad sense. The most valuable materials for the study of these sociological factors in disease are to be found in the records and reports of the Hospital Social Service Associations and in such volumes as Cabot's Social Service and Art of Healing, the Journal of Abnormal Psychology, and the like.

There are, beside the above mentioned aspects, others which are associated with industrial surroundings. In this group belong the subjects of industrial poisonings, vocational morbidity and mortality, and diseases of occupation. One thinks in such a connection with the allied problems of vocational guidance which are ones dealing, in part, at least, with the placing of individuals in industries, or divisions of industries, suited to their physical and mental make-up, for it is obvious that a person may be either physically or mentally harmed if he is placed at work for which he is not fitted. With this is again associated problems of the effects of fatigue as influenced by interest and pleasure, as well as those of mental retardation, and deficiency and moral delinquency.

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Intestinal Intoxications.

The term intestinal intoxication is one which has, at the present time, more clinical significance than pathologic. To the clinician the term means a series of symptoms which are associated with gastrointestinal abnormalities of almost any kind. It is a term which occupies

a place similar to that held, in the minds of many, by neurasthenia. In other words its significance varies with the physician or surgeon, and perhaps the point of view of the individual clinician is based upon his belief that the symptoms are due to the following:

1. The toxic effects of poisonous substances produced in the intestine and thence absorbed into the system. It may be said that this is a possibility although there is no definite experimental evidence. It is true that in the process of digestion of foodstuffs, especially the proteins, that poisonous materials are produced. These however are as a rule neutralized or inactivated by chemical combinations in the tissues during the process of absorption.

2. The toxic effects of poisonous substances produced by bacterial activity in the intestines. Such substances, for example, the ptomains, are extremely toxic. The amines also are exceedingly active poisons, and such aromatic substances as indol and skatol have been credited with grave disorders. As a rule, however, these substances are produced in too small amounts to be serious menaces, or, like indol and skatol, are chemically combined, inactivated and excreted. It may, however, happen that in occasional instances, as in ptomain poisoning, such substances found completely without the body, are introduced in sufficient amount to produce disease. It may also happen that chemical combination does not occur in the body.

3. The symptoms may be due to the action of endotoxins or exotoxins of the intestinal bacteria, which may be found within the intestinal canal and from there absorbed.

4. The symptoms may be due to the penetration of bacteria themselves which gain entrance to the tissues from the intestines.

As a rule the effects produced by the factors mentioned in groups 1 and 2 cannot be separated, nor can

those indicated in groups 3 and 4, because in the first instance bacteria are constantly present in the intestines and carry on their work of splitting the foods while the normal ferments are carrying on theirs, and, in the second instance, toxins are absorbed from the intestinal tract and cause changes in the organs, while in occasional instances, the bacteria also enter through the walls of the tract and are engulfed by the cells of the tissues where the endotoxins are set free and there they produce their pathologic effects. This is illustrated in the severe clinical complex called *typhoid fever*. In many cases of intestinal intoxication the symptoms are produced by organisms which are of less pathologic significance, for instance, the colon bacillus, and perhaps other bacterial forms. To such conditions Adami applies the useful term *sub-infection*.

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CHAPTER IV.

DISTURBANCES OF METABOLISM.

By metabolism we mean the sum of the chemical changes taking place in the tissues of an organism. One phase, which is concerned with ingestion and assimilation of food materials is known as anabolism. The other, concerned with the breaking down excretion and elimination is known as katabolism.

Metabolism is modified in either or both its phases by the quality and the quantity of the food, and also by conditions within the body which influence the cells and tissues in such a way that they are less able or more able than normal to make use of food. For instance, the quantity of food which is necessary to keep the body in a normal state of nutrition depends upon age, muscular activity, and climate, and upon certain other conditions some of which are inherited, some of which are acquired. Also some of the individual conditions are transient, some are permanent.

It is quite evident from superficial observation that a child uses more food compared with its weight than an adult. It is just as evident that an old man uses less than an adult in the prime of life. These variations are dependent upon the activities of the cells of the organism. In the infant and during childhood, growth is rapid, the individual is very active, and food is used rapidly, both for the production of heat and for the growth of the tissues. As age increases, the activities of cells, and of the organism itself, decreases, and not only is less food necessary, but less food can be utilized.

It is a matter of everyday experience that the active

person needs more food (other things being equal) than he who is sedentary. During muscular activity, more food is used in the production of heat. In the absence of muscular activity, the food that might merely be burnt becomes unnecessary, and therefore we may say, in a very general sort of way, that the needs of the body depend upon the amount of muscular activity. Of course this is not entirely true but it is sufficiently true to make a point of it. The food needs of the body are modified by age, and this depends in part at least upon muscular activity. They are also modified by the external temperature which surrounds the body.

Other influences which affect the use to which food is put within the body are (1) individual differences, which are difficult of description for obvious reasons, and (2) the influence of the ductless glands, which are only now beginning to be understood. It is perhaps true that the so-called individual differences are expressions of varying activities of the ductless glands.

We all know that some individuals eat very large amounts of food and remain slender, while others take small quantities of food and become excessively stout. In part such phenomena depend upon muscular activity; in part, upon certain not-understood conditions within the body which allow of storage of large amounts of fats. In some instances one or another mental type is associated with the physical condition. In some cases we believe that the internal arrangements within the organism are not properly balanced, and in some such cases we have reason to believe that the derangements are associated with more or less definite lesions, that is to say, with abnormal activities, of certain of the organs of internal secretion; for instance, the pituitary gland, the genital glands, the thymus, the thyroid, the adrenals and the pancreas.

When a person becomes stout, when he increases in

weight, it is obviously because he assimilates and holds a larger proportion of his food than he uses up in producing heat and other forms of energy. If he loses weight, it is because he uses up more food than he retains. Some individuals will do one or the other of these things, regardless of the amount of food taken. But the normal individual who holds his weight upon a normal diet can be made to increase in weight by increasing his food or by decreasing his muscular activity. He may also be made to lose weight by decreasing the food or by increasing his activity. He will also lose weight if he is not contented, if he is worried. Hence, the saying, "laugh and grow fat."

But aside from the question of quantity of food there is the very important factor of the *quality of food*. We know from our studies in physiology that a normal diet must be more or less balanced in its content of protein, fats and carbohydrates, salts and water, and we know that absence of any one of these constituents will produce greater or less change, or even damage to the organism, depending upon the length of time the lack is continued.

So much for the general external conditions of metabolism. Beside these there are the general internal conditions of metabolism which have been touched upon in the section on Intestinal Intoxications.

We know that during metabolism many substances are formed within the body—in the cells, and given to the blood—which if they were permitted to remain unmodified in the body would be extremely poisonous. We know that as a rule these substances are disposed of by excretion in the urine, feces, sweat, etc., usually after they have been chemically combined in such a way as to make them physiologically innocuous. We also know that certain—perhaps all—the cells of the body produce substances (internal secretions,—hormones) which serve a physiologic purpose, but which also, when they are pro-

duced in more than normal amounts, lead to serious disorders. It will be obvious that if such substances when produced in normal amounts serve a physiologic purpose, then the body will suffer as it is not supplied with adequate amounts. Here then, as in the case of food, we have disorders due to too much, and too little, internal secretion.

There is a final possibility that abnormal substances may be formed within the body, as a result of prevented activity of the cells. As a rule such substances are not of serious import.

It appears that disturbances of metabolism are the results of interruptions in the chain of physiologic transformation of foodstuffs and that these interruptions are the results of modifications of cellular activities which are, except in rare instances, the results of variations in the environment of the organism which result in certain instances in what we call hereditary, or congenital, individual differences.

According to the foregoing remarks, pathologic conditions the body may result from the following:

1. Failure of elimination.
2. Failure of one tissue to make physiologic use of the products of metabolism of other tissues.
3. Failure of chemical combinations.
4. Excessive production of otherwise physiologic materials.
5. Insufficient production of otherwise physiologic materials.
6. Combinations of two or more of the previous factors.

During metabolism, the constituents of the tissues are broken down into simpler compounds, many of which are acids. In the presence of a sufficient supply of oxygen these acids are present only transiently and are rapidly

decomposed or combined, and so become harmless. In the absence of a sufficient supply of oxygen they persist. When this happens a condition arises which we call *acidosis*.

Acidosis is present in greater or less degree in diabetes, anemia, starvation, inanition, and cachexia, fatigue (muscular or mental), following anesthetics, during pregnancy and fevers, and in uncompensated cardiac and respiratory diseases.

In certain abnormal circumstances, a condition of acidosis is associated with certain acids, particularly those belonging to the group of amino-acids. Such conditions are uremia, eclampsia, acute yellow atrophy and chloroform necrosis.

Anomalies of Metabolism.

Anomalies, as we usually use the word, are variations from normal which have no detrimental effect upon the organism. In the realm of the anatomic we speak of the presence of six fingers, or six toes, for instance, as anomalies. They interfere not at all with the health and life of the organism, although they may be inconvenient. In the same way, when we speak of anomalies of metabolism, we mean chemical phenomena as they occur in the organism which, though they do not appear in the perfectly normal individual, yet do not act to the essential disadvantage of the organism. Such anomalies are alkaptonuria, cystinuria, pentosuria. The former is characterized by the excretion in the urine of a substance (homogentisic acid) which normally is not present in the urine. Upon exposure to the air and light such urines become quite dark in color, even almost black. Cystinuria is characterized by the excretion in the urine of a sulphur containing material called cystin, which can be recognized by the microscope. Pentosuria depends upon the excretion in the urine of a pentose, a sugar, which may be recognized by chemical methods.

Somewhat analogous to these conditions is albinism, in which the body, even the hair, appears to be completely devoid of pigment. The causes of this lack of pigment we do not know.

High Temperature.

The regulation of the temperature of the body depends mainly upon two factors—physical and chemical. The

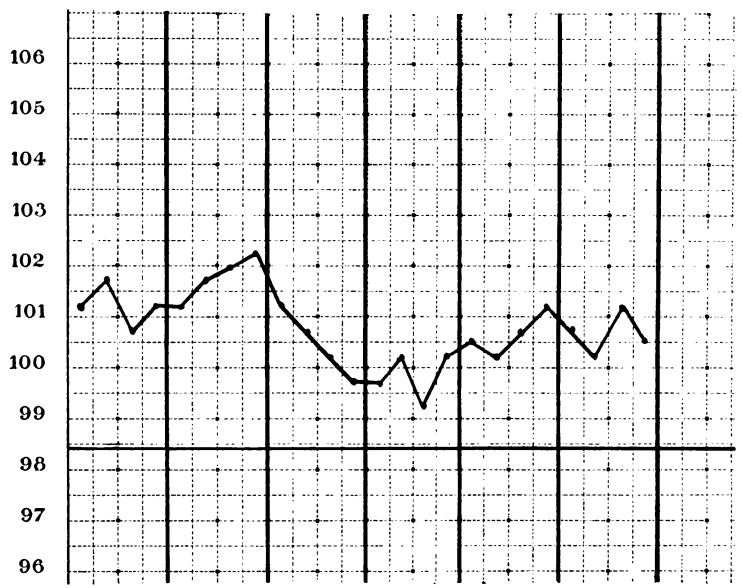

Fig. 2. - Continuous fever.

physical factor has to do with heat elimination and is largely bound up with the circulation and secretion from the skin. The chemical factor has to do with heat production within the body and is an affair of combustion (oxidations) of foodstuffs within the body. If heat production rises without a corresponding activity in the organs of elimination, the body temperature rises. The body temperature therefore depends upon the balancing of heat production and heat elimination.

Every activity of the body increases, temporarily, its temperature. Muscular exercise is especially active in this respect. During exercise more fuel is burned, and more heat is produced and must be eliminated, and so the blood vessels of the skin dilate, the face is flushed, and perspiration is increased. In this way heat is eliminated from the body and the temperature tends to keep its normal level. During such work, the rectal temperature may reach 38.3° (101°) without any evidence of discomfort.

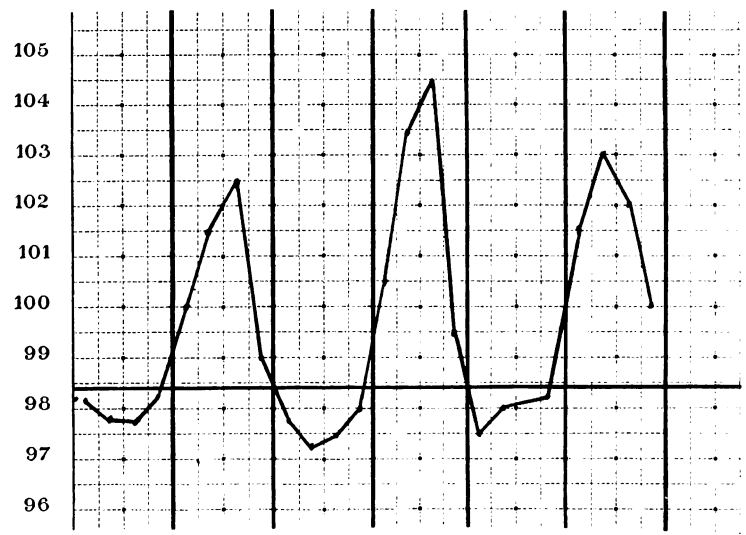

Fig. 3.— Remittent fever.

It is probable that the normal temperature curve owes its form to the effects of rest and activity.

Even after a hearty meal the temperature may rise to a slight degree. Hot and cold drinks of course modify the temperature.

More important perhaps than any other factors than exercise, are external temperature, humidity and breeze. These influence heat elimination chiefly for very obvious reasons. If the temperature surrounding the body is

high, less heat can be given off in a unit of time and so the body temperature tends to rise. This is especially true if the humidity is high, for the moisture on the surface of the body will not evaporate rapidly and so the cooling effect of evaporation is lost. If, on the other hand, a breeze fans the body, evaporation is more rapid. It has, for instance, been shown by workers in the tropics that

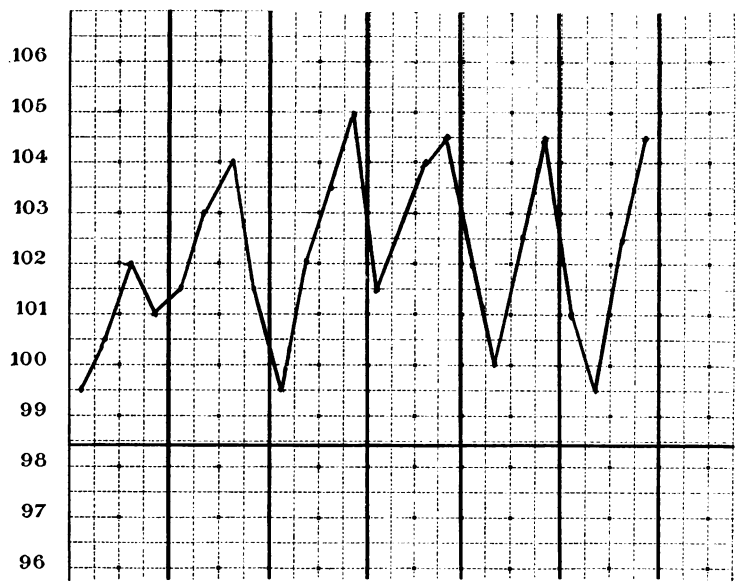

Fig. 4.—Intermittent fever.

the effect of even light breezes may counteract the otherwise almost intolerable heat of the glaring days.

Now, inasmuch as temperatures as high as 38.8° (101°) may be considered as falling within physiologic limits, and inasmuch as the normal range of body temperature in a healthy person lies between 96.8° (36°) and 99.5° (37.5°), and inasmuch as these upper figures are sometimes called fever temperature, we wish to know what "fever" is. Perhaps we might say that fever is a condition of abnormal temperature variation during which the

mean temperature of the body is raised. The mean daily temperature is about 37° (98.6°), or we may say that "fever is a term to include all conditions in which the normal temperature of the animal body is markedly exceeded for any length of time."

But fever relates to more than temperature alone. The person who works, physically, until his temperature reaches 101° (38.3°) does not feel any discomfort. The person who has a fever of 101° (38.3°) *does* feel discomfort. "The elevation of the temperature of the body is one of the usual signs of fever, but is not an essential one. As a matter of fact, fever as a rule is the result of infection by bacteria, and is a complex thing, associated with chills, headaches, feelings of malaise, nausea, vomiting, pains in the limbs and muscles, dizziness, and often with a rise of temperature (pyrexia). It is quite different in all its appearance from the rise of temperature (hyperthermia) caused by external heat (sunstroke—insolation), lesions of the nervous system, and poisonous drugs.

In speaking of the temperature during fever, the following terms which are sometimes used, are illustrative:

Slight fever 100.4°-101.12° F. (38-38.4° C.).

Moderate fever 101.3°-102.2° F. (38.5°-39° C.) in the morning, rising to 103.1° (39.5°) in the evening.

Considerable fever 103.1° (39.5°) in the morning, and 104° (40°) in the evening.

High fever 103.1° (39.5°) in the morning, and 104.9° (40.5°) in the evening.

Hyperpyrexia 107.6° (42°) or more.

Fever is divided into three stages, the initial or pyrogenic stage; the fastigium or fastigial stage; and the defervescence or defervescent stage. The first stage may be short or long; an hour or two—malaria, or lasting one or several days as in typhoid. The second stage may be very brief or very long. The third stage also may be quite short (crisis) or the fall of temperature may occur gradually (lysis).

A *continued fever,* as one in which the daily tempera-

ture changes, although they occur at a higher level, are little or not at all greater than in health. (Typhoid, pneumonia.)

A *remittent fever* is one in which the temperature changes are exceedingly irregular, and during its course the normal line may be touched (suppurations; pyemia, tuberculosis with secondary infection).

Intermittent and *recurrent* fevers are characterized by series of initial fastigial and defervescent stages as in malaria, relapsing fever, etc.

In the first or initial stage, the patient complains of cold, and suffers a chill. His skin feels cold and clammy though the thermometer introduced in the rectum will show that the internal temperature is above the normal. The onset may be rapid or slow, and the duration of the rigor may be brief or prolonged. Often, at the onset of a fever, there is no chill but merely a period of depression during which the temperature rises. The *feeling* of cold, in spite of these increased temperatures depends upon the fact that the sensations of heat and cold arise in the skin, at the onset of a fever the surface temperature commonly falls.

In the second stage, into which the initial one merges, the skin becomes hot and flushed, and instead of feeling cold the patient feels hot, and correspondingly thirsty.

The third stage, as has been said, may be short (crisis) or prolonged (lysis). In this first case the temperature falls very rapidly and the fall is accompanied by profuse perspiration.

Fever, we believe, is due to the production of too much heat in the body and is caused by the action of bacteria or their products. It is a compound of heat accumulation by over-production, and intoxication by poisonous substances.

In sunstroke (insolation) on the other hand, the cause of the symptoms is the heat rays acting upon the body.

These rays act first by heating the body so that its chemical processes are quickened and more heat is therefore produced to the point where elimination by evaporation or radiation is no longer possible, or to the point when the water supply of the body is so depleted that the skin is no longer capable of secretions for evaporation. When the air is hot, still and humid, the body cannot lose its heat, and then if physical exercise is persisted in, the internal temperature of the body may rise to very high points. It is possible that heat exhaustion is due to gradual depletion of the water of the body without equivalent loss of heat, and that heat stroke is due rather to rapid accumulation of heat with or without water loss.*

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The Internal Secretions.

The organs of the body are very commonly looked upon as independent of one another, each doing its own work with no other than an anatomic relation to the others, or

*For a discussion of the effects of drugs on the temperature, see Pembrey and Ritchie's General Pathology, p. 534.

only related by means of the nervous system. How incomplete such a conception must be one may readily appreciate if he remembers that the function of the vascular system makes it fully as vital a correlating mechanism as is the nervous system. The blood vessels are channels by which food is carried to the various cells of the body, but they are likewise, in a sense at least, channels by which cellular wastes are carried away. In whatever way we may interpret the word *wastes*, the conception does not necessarily mean that such materials are valueless in the general economy. What is waste to one organ may be food for another. A waste may be a serious matter only when some group of cells which make physiologic use of it are absent. It therefore is evident that each organ is apt to have an influence on other organs through its metabolic products which are secreted (or excreted) into the venous blood or into the lymphatics. There are many evidences of the truth of these statements, but they are most frequently studied in connection with the ductless glands,—the glands of internal secretion. In the secretion of these organs there appear to be particular chemical substances (one of which, adrenalin, has been isolated, and even synthetically prepared) that produce characteristic physiologic effects. These substances are the *hormones*. They are parts of the chemical coordinating system of the body. This system determines the direction of reactions. The nervous system determines the speed. Each system modifies the other.

If these secretions are of such importance it might be expected that the systemic effects of increased or decreased activity of the organs of internal secretion would be striking, and it is true that they are. Such effects may be the results of excess or loss of the specific materials of the secretions, or they may be due to the lack or modification of a specific substratum upon which to act. There is evidence in experimental work that the effects are not

simple, i. e., that they are not the result of damage to one organ, and modification of its secretion, but the result of interference with the interrelated activities of such organs. As yet we know next to nothing of the methods of interference, or of the conditions upon which these glandular effects depend, whether in antecedent metabolic disturbances, infections, intoxications, or in primary derangements of the central nervous system. "In the case of the thyroid, for example, exophthalmic goiter with its outspoken nervous and psychic manifestations was formerly regarded as essentially a sympathicogenic or psychogenic disorder, and among others Biedl has again come to support this view as opposed to Moebius. Unquestionably the mental repose of successful psychotherapy on the one hand, and on the other, such a radical measure as the blocking of secretory impulses to the gland by cervical sympathectomy, have both served in many cases almost as effectively as the now popular extirpation of the hyperplastic gland itself." It is in connection with studies of the effects of nervous impulses in the production of secretory effects that we need to recall the older expression "phlegmatic and nervous disposition, or diathesis, or constitution." These same peculiarities appear now as sympathetico-tonic and vago-tonic, and indicate the same old misunderstood fact that one individual reacts with abnormal quickness to an impulse, particularly an emotional one, while another reacts less quickly than normal. On the other hand there seems to be no doubt that certain intoxications produce important effects upon certain, at least, of the ductless glands. In such cases we may perhaps search for the causes of vago-tonicity or sympathetico-tonicity in infections or gastrointestinal intoxications. Schiefferdecker goes to the extreme in saying: "Internal secretion determines the effects which the products of metabolism excreted by the nerve cells during the simple processes of nutrition, will exercise

upon other nerve cells and the end organ, such activity being called 'trophic.' It also determines the effect which the products of metabolism excreted in the course of specific activity will produce, and this effect is known as 'irritation' or 'stimulus'." Whatever one may think of such a statement it indicates, as Biedl says, the trend toward the ultimate explanation of physiologic and pathologic correlationships in terms of chemistry, and it also indicates the value and extraordinary interest which is attached to the glands of internal secretion.

It will be noted that the internal secretory organs are in a triple alliance. One other member, the nervous system, we have mentioned. The other is the sexual system. During normal growth there are certain psychic events which accompany sexual development. Morphologic and, certainly, secretory changes in the ductless glands occur during the same period. It is no more than one might expect, then, that experimental work indicates a chemical connection between these three systems, and that while the reproductive organs exercise an influence upon the nervous system, other organs which also influence that system may affect the reproductive glands. There is an interlocking directorate, and it seems "probable that a disorder primarily involving any member of the ductless glands series, leads not only to peculiar somatic alterations but also to an accompanying and characteristic mental change," with, frequently, a sexual phase. So, says Cushing, "it is quite possible that the psychopathology of everyday life hinges largely upon the effect of the ductless gland discharges upon the nervous system." But, we may add, these effects may lie in an increased stimulability on the part of the tissues toward nervous impulses, or an increased susceptibility of the elements of the nervous system to otherwise subliminal or unproductive stimuli.

"It is more or less customary, largely because of their

effects upon metabolism, to classify the internal secretions as inhibitory (or assimilative) and stimulant (or disassimilative), the one influencing the anabolic phase of metabolism, the other the katabolic. They are also referred to as growth producing and growth retarding. In certain cases the effects of these secretions are felt throughout the whole span of life; in others they play but a transient part, at one or another age or period. Not infrequently their influence is shown by special effects on certain organs; again they modify general nutrition; or in still other cases they produce purely psychic effects."

In the foregoing paragraphs the emphasis has been placed upon the idea that the effects produced by disorders of the organs of internal secretion are the results of overabundance or lack of the specific chemical products of these organs. This is not the only tenable point of view.

It is believed by many that these organs have also what is called a detoxicating action, and that in cases in which there is insufficiency the effects produced in the organism are rather the result of the action of toxic substances which, normally, are destroyed or modified by these organs. This idea is applied chiefly in the case of the thyroid. In this connection it may merely be suggested that local detoxication is rendered doubtful by the fact that in mammals the effects of thyroidectomy may be removed partially by feeding of desiccated gland substance. Therefore it seems more plausible to conceive that action of the secretion of the thyroid is effective, in a general metabolic way, in increasing the activities of the other organs and tissues of the body to a point where toxic substances are cared for.

However, so far as we know, the main feature of all disturbances of the glands of internal secretion is that they are not simple. The effects as shown in symptoma-

tology are the results of the action of what has been called the "interlocking glandular directorate which profoundly influences metabolism and the mental and sexual life" (Dunn). Therefore it may be said that while it is simplest to discuss the effects of the organs of internal secretion under the heads of the different organs, it is to be remembered that the complexes associated with these effects are, as a rule, polyglandular ones.

Fig. 5.—Goiter.

The Thyroid and Parathyroid Glands.

There seems to be no conclusive evidence at present that there is any essential difference between thyroid and parathyroid tissue, for it has been shown that all morphological transitions occur between the two. In speaking of the thyroid gland we therefore mean to include the parathyroids.

The internal secretion of the thyroid acts chiefly as a

dissimilatory hormone insofar as it increases katabolism and therefore tends to accentuate normal function. This effect is seen in various activities—in protein metabolism, in the effect upon cardiac activity, and especially, perhaps, upon other internal secretory organs (hypophysis, adrenals). Certain phenomena suggest that the thy-

Fig. 6.—A case of congenital myxedema. (After Kassowitz.)

roid secretion also possesses an inhibitory function, and that therefore it contains an assimilatory hormone. The promotion of skeletal growth, the development of the sexual glands, the limitation of the internal secretion of the pancreas, are evidences of such activity.

The experiments of Gudernatsch indicate that "the

thyroid has the power to excite differentiation, but it lacks the power to cause growth." At the same time it does not seem to have the power of preventing growth. If these experimental results, which were acquired by

Fig. 7.—A case of hypophyseal destrophy in hypopituitarism. Froehlich's type of dystrophia adiposo-genitalis. Caused, it is believed, by lack of pituitary secretion. (After Falta.)

work in tadpoles, be true for the human being, then the effects which are referred to as inhibitory are not thyroid effects, but effects resulting from the action of the secre-

tion of the thyroid on other organs. It is believed by some upon very good evidence that the parathyroids are concerned in calcium metabolism, and that they are responsible for the symptom-complex known as tetany.

Diseases of the thyroid are associated with:

Graves' disease (exophthalmic goiter).
Cretinism.
Infantilism (infantilismus myxedematosus, Brissaud).
Delayed maturity.
Achondroplasia (fetal rickets).
Myxedema.
Tetany.

The Thymus.

It seems possible that the thymus exercises, through its internal secretion, important effects upon growth and that it has an inhibitory influence upon the development of the genital glands. Appearances seem to indicate that involution of the thymus is consequent upon sexual maturity. The work of Gudernatsch suggests that the thymus has the power to stimulate growth, but lacks the power to excite differentiation and not only that, but thymus feeding seems to suppress differentiation.

Lesions of the thymus are associated with:

Status thymico-lymphaticus
Precocious adiposity
Certain cachectic states
Exophthalmic goiter
Skeletal changes (rickets?)
Dwarfism
Achondroplasia

The Pituitary Gland.

The pituitary gland has effects upon general processes which in some respects are quite similar to those associated with the thyroid gland. In young animals suppression of function is manifested in an increase in the body fat together with hypoplasia of the sexual glands, and arrested development. The influence upon the sexual

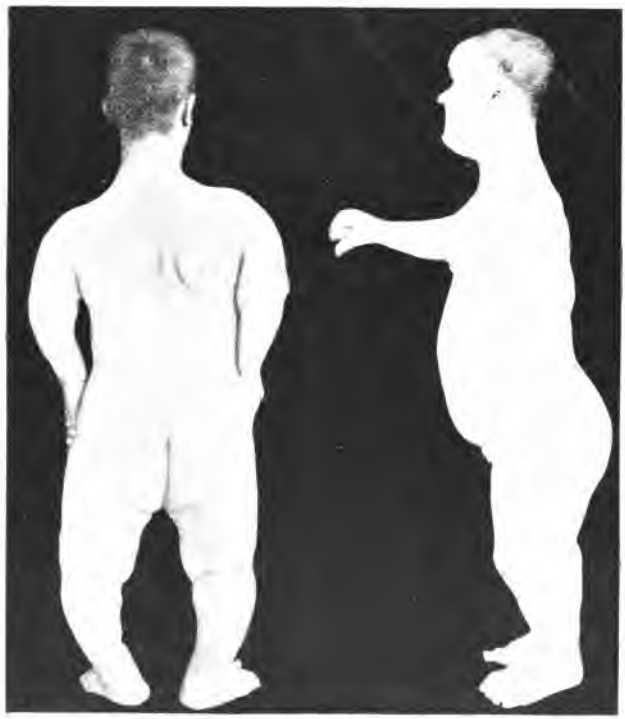

Fig. 8.—A rhoodredestrophic dwarf. (After Falta.)

glands is seen also in older animals in which partial destruction of the anterior lobe is followed by atrophy of the genitalia. It seems evident that "the pituitary body and the germinal glands are protagonistic. Hypophyseal insufficiency and lowering of the activity of the reproductive functions go hand in hand," and also "a libidi-

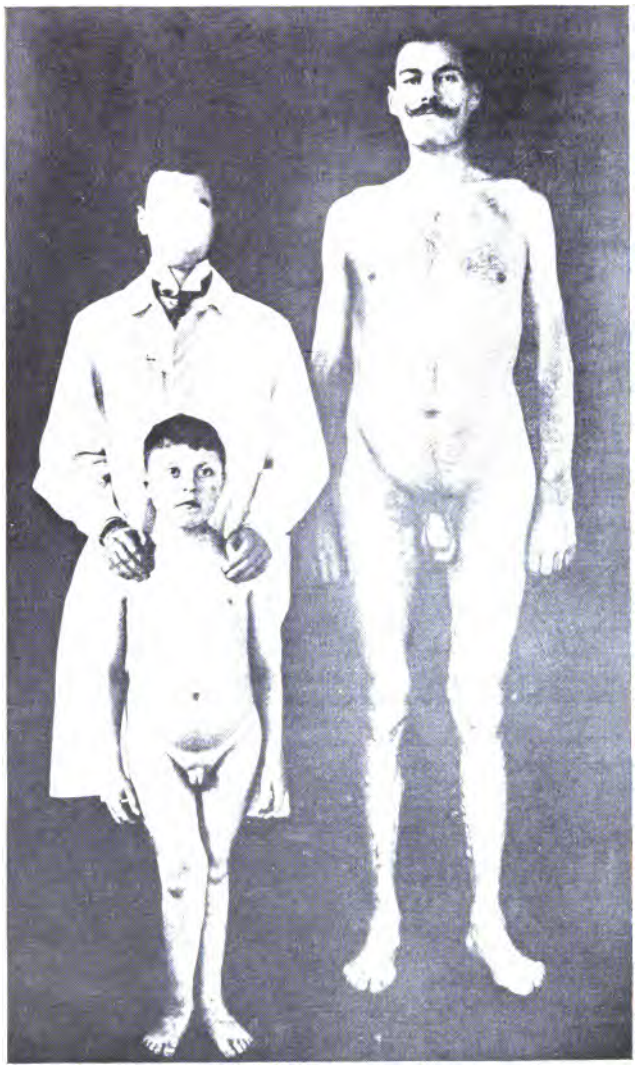

Fig. 9.—A case of giantism, a hypophyseal dwarf, and a normal man. (After Falta.)

nous tendency often accompanies states of secretory hyperplasia."

Lesions of the hypophysis are associated with:

Acromegaly
Gigantism
Diabetes insipidus
Diabetes mellitus
Infantilism
Dystrophia adiposo-genitalis (Froehlich).
Cachexia hypophyseopriva.

It is to be recalled that lesions of the thymus are apt to be associated with dwarfism, while those of the pituitary and thyroid are associated with infantilism. These two conditions are frequently confounded. The important difference is that mental changes are not associated with the former. Dwarfism is a defect of size and appears because growth ceases at some stage of development. A child may be normal at birth and then growth may cease (*nanosomia infantilis*), or it may be defective as to size from the start (*nanosomia primordialis*). The term infantilism, as defined by Laséigue, "is a disturbance of development, the salient feature of which is the persistence in both the mental and physical state, of infantile characters." In the term, however, has been included certain cases in which arrested development has resulted from nutritional derangements, and from disease of the blood vessels, brain, etc. This form is known as *infantilismus dystrophicus* of Lorrain. It may appear as the result of hypoplasia of the vascular system, in hereditary syphilis, after alcoholism and other forms of chronic poisoning in the parents; in primary cerebral disease, as a result of infectious diseases contracted in early life (tuberculosis, pellagra); metabolic derangements (chlorosis); cardiac diseases (pulmonary and mitral insufficiency); and finally as the result of unhygienic surroundings and insufficient nourishment in early childhood.

From the fact that lesions of numerous glands of internal secretion are associated with infantilism it is probable that this complex is associated with lesions of more than

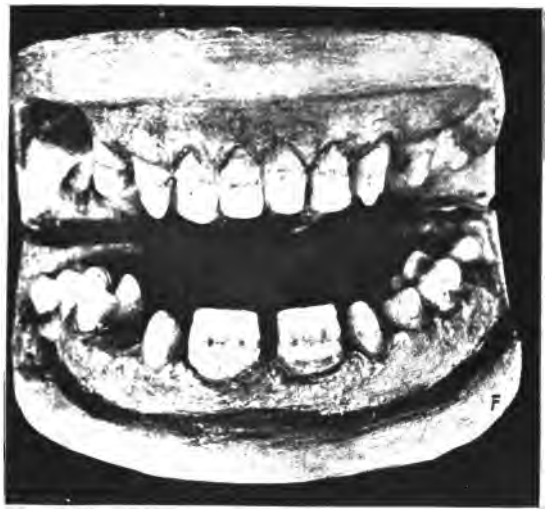

Fig. 10.

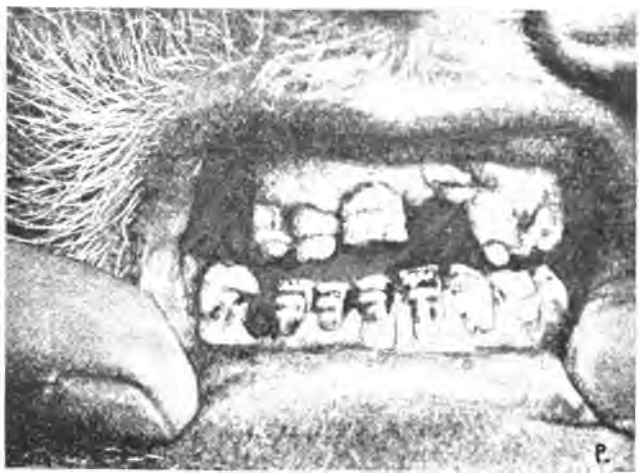

Fig. 11.

Figs. 10 and 11.—Examples of enamel defects in cases of tetany. (After Falta and Phelps.)

one gland and that the distinguishing characters of various forms of the complex are connected with single glands. Infantilism is therefore a polyglandular affection.

The Adrenals.

The adrenals like the pituitary are composed of two functional parts. These are the medulla and the cortex.

Fig. 12. - A case of mongolism standing beside a healthy child. (After Falta.)

The medulla is the chromaffin portion of the organ and is closely associated with the sympathetic nervous system. The cortex is quite similar in structure and appearance to the corpus luteum, and seems to be closely related, functionally, to the sexual glands. The medulla

is a part of the chromaffin system of the body, and is the portion of the gland which (like the other chromaffin tissues) produces a vasoconstricting substance known as adrenalin. Variations in its activity have been associated with Addison's disease, with conditions of low vascular tension, on the side of insufficiency; and with glycosuria, arteriosclerosis, cardiac hypertrophy and conditions characterized by high vascular tension, on the side of hyperactivity. Cortical variations have been found in association with periods of heat and rut, sexual precocity

Fig. 13.—The facial expression in mild myxedema. (After Falta.)

and with defective sexual development. There is reason to believe that a close relation exists between the adrenals, pancreas, thyroid, pituitary and sexual glands. In the fact that the internal secretory activity of the pancreas is inhibited by adrenalin lies an intensely interesting

application of the ideas of Eppinger and Hess, for the pancreas is under the nervous influence of the vagus, while the adrenals are under sympathetic influence. The fact that adrenalin increases thyroid activity while at

Fig. 14.—To give some idea of the expression and position of the fingers in tetany. Tetany is supposed to be associated with disturbances of the parathyroid glands. (After Falta.)

the same time it decreases that of parathyroids, suggests, following the same reasoning, that the latter are under the influence of the vagus.

The Pancreas.

The internal secretion of the pancreas seems to be an important factor in carbohydrate metabolism, though just what part it plays is by no means certain. It is possible that this secretion contains a substance or substances which make it possible for the tissues to use sugar. Stanley calls attention to the fact that an isolated heart from a diabetic animal, when perfused with blood *plus* glucose, is unable to consume the glucose; but in adding an extract of fresh pancreas, the sugar is consumed. How this happens we do not know. Biedl says the most probable assumption is that the active substance is ferment, which inhibits the diastotic conversion of glycogen into sugar, though it does not prevent the storing of glycogen. Absence of the hormone permits unchecked splitting of glycogen.

The Pineal Body.

Of this gland we know too little. It seems to be true however that whatever changes occur must present themselves during the period during which the gland is active, for it, like the thymus, undergoes early retrogressive changes. Lesions in it have been associated with obesity and macrogenitosomia precox. Recent experimental work of Dandy indicates that the pineal body (epiphysis) has no physiologic importance.

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tion, and this depends upon certain physico-chemical conditions. Abnormal constitution will just as surely bring about abnormal absorption, and, perhaps, what was not absorbed yesterday will be absorbed today and illness will result. Normal constitution of cells and organs depends upon normal activity, and so, as Cohnhein said, "The regular circulation of blood of normal quality and the physiologic activity of the organs are equally necessary."

The quality of the blood we wish to discuss in relation to physiologic activity. The regularity of the circulation we shall discuss at another time. But first it will be useful to say some words concerning the quantity of food.

As you know from your consideration of growth, quantity of food may mean two things. It may mean the quantity available, or the quantity needed. Atrophy, you remember, may occur in the presence of an abundant supply of normal blood, providing the cells are inactive —which is to say, are in a condition (physico-chemical) which makes them unable to take food. On the other hand, atrophy will just as surely occur in the absence of a sufficient supply of foodstuffs.

The quantity of food needed by an organism depends, other things being equal, upon activity. It is for this reason more than any other, that the normal necessary amount varies with age, and climate. In growth the whole organism is active; the food is rapidly consumed and transformed into heat and other forms of energy and the supply must be frequently replenished. In old age, the opposite is true, the individual is less active; combustion is slower, and therefore less is needed. A cold climate tends to increase activity, and therefore the food demands are increased. Hot climate conduces to inactivity and to decreased demands, even though it hastens combustion.

And yet we hear it said frequently enough that we eat too much, or we eat too little. Why do we eat too much, or too little, and what happens when we do either? Sometimes we eat too much because we haven't anything else to do and because we like the taste of food—or of some foods. Sometimes, because we are completely, mentally, contented, and being contented we are inactive. Nothing stimulates us to activity. Sometimes there is something wrong in our physiologic make-up, so that we experience the feeling of hunger when we should not. But sometimes we eat too little because we are discontented and the taste of food is unpleasant, or because we cannot have pleasant food. We may be worried, and being either discontented or worried, our appetites are small and our activity increased. We are restless and burn more food than we otherwise would. Sometimes, again, our physiologic make-up is deranged and we have no desire for food, or desiring it, cannot use it or, sometimes, retain it.

And then, in either case, what happens? We "laugh and grow fat" as the saying is, or we "worry ourselves to a skeleton." We become obese, or poorly nourished, or in the end we starve.

There are two main types of obesity—physiologic and pathologic. The former is seen in infants, and in youth just before the time of puberty. The latter occurs as a result of lack of exercise—of physical inactivity, and as a result of disturbances of the function of one or more of the ductless glands. It is quite possible that the obesity that precedes or accompanies puberty is due to internal secretory activities. Certain types of familial and racial obesity may be either physiologic or pathologic,—which, we do not know. All, however, of whatever type, depends upon a storage of fats in the tissues and this in time may be due to deficient powers of oxidation within the body or to the presence, along with ordinary food-

stuffs, of more easily oxidizable materials, such, for instance, as alcohol. Opposite to obesity is emaciation, malnutrition, undernourishment, and starvation, due not merely to the using up of the transient supplies, but also of that other source of heat and energy that should be used only in occasional times of need,—the fats and proteins of the body. Poorly nourished children may grow in stature though not in weight, and during such abnormal growth the bones grow at the expense of the internal organs. It is only in the last stages of emaciation that growth stops in children, but even then the power of growth is not lost but returns with proper feeding (Arons: Jour. Am. Med. Assn., 1911, lvii, 1619). But under certain circumstances growth is retarded, though mental development proceeds—a condition we call infantilism, and this leads us to call attention to the interesting fact that in starvation the vital organs are spared at the expense of the other organs. The brain even at the last shows little or no change.

Finally, in this connection, let me emphasize that either overeating or the refusal of food is not important. It is the cause of either.

This may all be epitomized as follows:

1. Normally anabolism should equal katabolism.
2. When anabolism is greater than katabolism, obesity results.
3. When katabolism is greater than anabolism, wasting, emaciation, inanition and starvation result.

Beside obesity there are more serious things which happen as a result of overeating. Various sorts of gastrointestinal disturbances are not infrequent. The overloading and distention of the stomach, together with the irritant effects of much food; the continuous or overstimulation of the gastric secretory apparatus; the fermentative changes in the food which, in large quantity, is with difficulty saturated and sterilized by the normally pro-

tective acid gastric juice; and similar effects in the intestines. All of these result in symptoms which are grouped together under "gastrointestinal autointoxications" or mere "indigestion." Such conditions are expressions of irritation of the gastrointestinal organs, of subsequent and consequent inflammations, and of the absorption of abnormal products or products abnormal in quantity, which may act as poisons when carried to other organs. We shall speak of these conditions at another place (see Intoxications). Faber, as an example of what one may think of the importance of too much food, says, regarding overeating, that he is convinced that many of the morbid conditions credited to the "uric acid diathesis" are in reality the effects of overeating. He has tabulated a large number of corpulent and normally nourished individuals and calls attention to the preponderance in the former group of certain types of rheumatism, lumbago, varices and constipation. The mortality from apoplexy, heart and kidney disease, is also higher in this group. He calls attention to the particular value of restricting the diet in such individuals.

While the quantity of food needed by the body is important, the quality of the food is still more important.

We are told that to continue in health, the body needs proteins, carbohydrates and fats, and that these serve in part for tissue building, i. e., growth (proteins), and as sources of energy (carbohydrates and fats). In a way this is true, but in the past few years Osborne and Mendel especially have shown that mixtures of chemically pure proteins, carbohydrates and fats, together with the normal salts and water, while they will sustain life, are not able to promote growth. Osborne and Mendel found the necessary stimulus for growth in milk whey, and in extracts of tissues, and, they found that these materials would be effective in such small amounts that their action could not be accounted for on the basis of oxidations.

More recently Funk, studying the tropical disease beriberi and its congeners, has extracted similarly effective substances from yeast, rice, etc., and the extract he calls *vitamin*. Not only have these things been discovered, but Osborne and Mendel have found that proteins of different origins have different nutritive values. So you see the quality of food is really decidedly important. Perhaps it is the quality of boiled milk and not the digestive variations in children which causes rickets and scurvy. Pasteurized and boiled milk are not as safe as uncooked milk, and yet all the original constituents are present. Holst and Froehlich fed guinea pigs with only cereals or bread, and produced scurvy in the animals. If fresh carrots and cabbage were fed, the animals remained well, and these vegetables acted in curative fashion if fed to scorbutic pigs. If, however, the vegetables were cooked at 110-120°, the curative power was lost.

There is a great group of diseases—i. e., clinical complexes—which seem to be due to qualitative changes—the diet. Beri-beri, scurvy, and rickets have already been mentioned. Goiter, pellagra, certain forms of neuritis, and gout, are possibly other members of the group. Perhaps certain of the anemias also are. In the case of beriberi it is interesting to recall that the complete removal of the husks in the process of polishing the grains produces a grain which used as an exclusive article of diet results in the disease. It has been noticed that the daily use of milk has been reported as useful in preventing pellagra; that fruit acids and salts prevent the occurrence, and hasten the cure of scurvy.

Schaumann calls attention to the minute amount of certain necessary substances in the diet. He says that they are present in most articles of diet but are readily removed and destroyed. Rice and other cereals lose them by polishing, and they are destroyed in other articles of food by heating above a certain temperature, or

by long cooking, sometimes by desiccation and by pickling, by boiling in alkalin water, by moulds and even in some cases, by the intestinal bacteria. The disturbances following loss of these materials, he says, differ in different organisms. Herbivora develop scurvy; omnivora, scurvy and neuritis; and goats, monkeys, fowls and pigeons, multiple neuritis. The practical conclusions are that the diet of man must comprise, beside the classical protein, fat and carbohydrates, salts and water, these unisolated substances. The protein must be one which contains tryptophan. As Osborne and Mendel have shown, a protein cannot be called a nutritive one if it lacks tryptophan (gelatin, zein). Tryptophan, Mendel says, is indispensable for life; lysine, for growth.

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CHAPTER VI.

DEGENERATION—PIGMENTATION —CALCIFICATION.

Degeneration.

When we speak of degenerations we have reference to a group of phenomena which characterize the presence of abnormal amounts of normal substances, the presence of normal substances in abnormal physical conditions, or the presence of abnormal substances within cells.

Fat is a common constituent, and a normal one, of all cells. In most cells it is not visible even under the microscope, This is true, for example, of heart muscle cells and kidney cells. In some cells it is commonly and normally visible, for example, in liver cells, and in the ordinary fat cells of the subcutaneous tissue. When fat appears in such a form or amount in kidney or heart cells, so that it can be seen, we speak of *fatty degeneration.* When it appears in the liver cells so that there seems to be more than a normal amount of visible fat we speak of *fatty infiltration.* Fatty degeneration then applies to the occurrence of fat where no fat should be visible, and fatty infiltration means an increase of fat where some fat might be expected. Fat appears in cells and tissues when the oxidations of the body are not sufficient to burn it, which may be the result of too great a supply of fat, or it may be due to deficient activities of the cells.

There is a certain condition which we call *cloudy swelling* on account of the fact that tissues so affected are swollen, and at the same time are not as clear, or translucent as they are under normal conditions. Such tissues have a "boiled appearance,"—they resemble, in a

way, a piece of tissue which has been dropped into hot water. Under the microscope the protoplasm of such tissues has a finely granular appearance, which is due to the fact that certain of the proteins which compose protoplasm have coagulated and appear as granules, soluble in dilute acids, or alkalies, in the otherwise clear protoplasm. From the fact that very small amounts of dilute acids will produce cloudy swelling we may argue

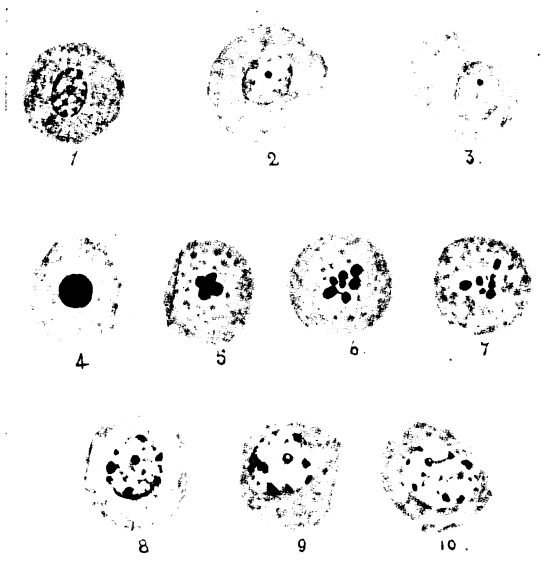

Fig. 15.—Cell degeneration. *1-3*, Karyolysis; *4-7*, Pyknosis, hyperchromatosis, and karyorrhexis; *8-10*, Karyorrhexis. Cloudy swelling is present in all of these cells. (Beattie and Dickson.)

that under certain conditions in the body acids accumulate, cause the protoplasm to take up water (swelling) and, at the same time, cause some of the proteins to coagulate.

Like cloudy swelling, the appearance we call *hyalin*, *colloid*, and *amyloid*, in cells and tissues, are also due to abnormal states of the proteins in the tissues. Connective tissues may appear hyaline (translucent); if it be also viscid or gluey, we speak of colloid; if it gives certain of

the starch reactions we call it amyloid. Tissues are said to undergo hyalin, colloid, or amyloid degeneration when they answer to these descriptions.

When cells or tissues die we speak of *necrosis*. Sometimes cells die as a whole, sometimes all the cells in a tissue die, and sometimes only part of a cell dies. When a group of cells die leaving their ferments still active so that the tissue is more or less softened or digested, we speak of *autolysis*. It is autolysis which goes on in pneumonia when the exudate of cells in the alveoli of the lungs is softened. It is autolysis which causes the central part of an abscess to soften so it can be squeezed out. When autolysis does not occur the material from the dead tissue may become somewhat dry and granular like cottage cheese. Then we speak of *caseation*. When a whole part of the body dies as a whole—like a hand or a leg, we speak of *gangrene* (because of the color) though the process is still necrosis. If the gangrenous part becomes dry and mummified, because the moisture is evaporated from it, we speak of "dry gangrene." If it remains moist, and becomes infected, we speak of "wet gangrene." Death of bone is commonly called "*caries*."

There are other forms of degeneration which are associated with abnormal amounts of certain substances within the cells. For instance we speak of *mucoid* degeneration and mean that more mucin is present than should normally be. When tumors show a high degree of mucoid degeneration or infiltration we call them myxomas; when, as in certain forms of disease such as those due to interference with the thyroid gland, the connective tissues, particularly the subcutaneous tissues, contain too much mucin, we speak of *myxedema*. In the one case the mucin is of epithelial origin, in the other of connective tissue origin. *Glycogenic degeneration* occurs when more than the usual amount of glycogen appears in cells; *soapy degeneration* when soaps appear; and *myelinic* or

lipoid degeneration when the lipoid or the myelins of the nerves or central nervous system undergo retrogressive transformations.

Pigmentation.

Under certain conditions foreign substances enter the body, are taken up by the cells and held in the tissues which are colored by reason of these substances. A person who lives in a dirty atmosphere, one like that of a large city, breathes into his lungs the small particles of carbon that are always present in the smoke which mingles with the air. These particles enter the lungs and are taken up by the cells of the tissue, the phagocytic cells, which carry them sometimes to the neighboring lymphatic glands, sometimes only into the neighboring connective tissue. The result of this is that the lungs become permanently blackened by the insoluble carbon. This condition is one of the *conioses*, or "granule diseases," and is specially known as *anthracosis*. In workers in iron, particles of that metal take the place of the carbon, and we speak of *siderosis*. In workers in clay, particles of that substance enter the tissues and we have *silicosis* or *chalicosis*. Pigmentation with silver, from overuse of silver salts, is called *argyria*, and pigmentation with lead occurs in plumbism.

In another group of circumstances the pigmentation is the result of excessive production, beyond the possibility of excretion from the body of pigmented bodies which stain the tissues. Sometimes the staining is due to interference with the excretory pathways, as in jaundice of the ordinary "yaller janders" type. According to the process such forms of pigmentation as *melanosis* appear, due to the deposition of melanin in the skin. The pigmentation of sunburn is due to localization of melanin. The color of freckles also is due to melanin. Generalized jaundice we speak of as *icterus;* jaundice

due to breaking up of the blood pigment is hematogenous jaundice.

Calcification.

Calcification under pathologic conditions is analogous to that which occurs under normal conditions, for instance in the calcification of membranes to form the flat bones of the skull.

When tissues die (undergo necrosis) several things may happen. The dead tissue may become liquefied and be removed or it may be replaced by fluid which remains as a cyst. The dead tissue may become infected by bacteria and an abscess results, or in the dead tissue lime salts may be deposited. This is what happens very frequently in tuberculous lesions, in various organs, especially in the lymph glands and in the lungs. Such areas are calcified. Sometimes dead bones are completely organized and scars are formed, and sometimes the scar tissue becomes calcified. Sometimes as organization of dead tissue goes on, calcification accompanies it, and the process goes on in such a fashion that bone is formed, and then we speak of *ossification*.

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CHAPTER VII.

INFLAMMATION.

Every one knows something about inflammation. Every one knows, for instance, that a conjunctiva that is intensely congested, that is painful, that produces a more or less serous discharge, is inflamed. Every one knows that a "boil," otherwise technically known as a furuncle, is the seat of a localized inflammatory process, and when one knows this he is immediately aware of the cardinal symptoms of inflammation, which Celsus, perhaps, first wrote down for others to read, namely, *heat, redness, pain and swelling*—calor, rubor, dolor and tumor. One is also aware that, because these four cardinal symptoms are present, something must be wrong with the parts of the affected tissues. With normal blood vessels there should not be this increase of redness and of heat. With normal tissues and normal processes there should be no pain and swelling. Something else is wrong. The function of the parts is abnormal. And so a fifth symptom has been added to those of Celsus, namely, *disturbance* of *function*—functio læsa.

Inflammation is a process by which the body reacts to injury. It is best described by Cohnheim in the following paragraphs.

"If you withdraw a loop in intestine from the abdomen of a rabbit and expose it to the air, it, together with the vessels, ultimately perishes, but death is far from instantaneous—rather a comparatively long interval must elapse before this point is reached, and during it the disorganization of the tissues and vessels progresses little by little till they finally die. If you cut off the circulat-

ing blood from a part and its vessels, necrosis sets in, but here again, as you know, a very considerable period passes during which the tissues, in specie the vessel walls, become gradually disorganized. At a temperature of from 36° to 38° C., the life and function of the blood vessels are regular and normal, at one of say 60° C. they are certainly destroyed. Now, if you expose a vascular part to a temperature somewhere between these extremes, though it does not die, the heat is not without its effect on the constitution of the vessel walls. Lastly, in order

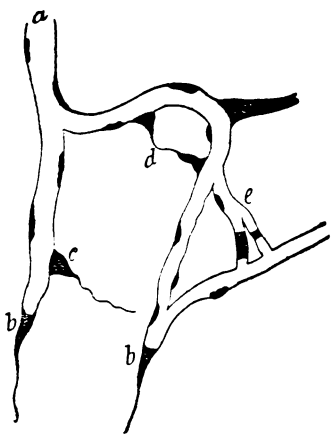

Fig. 1.—Formation of new blood vessels, as seen in the tail of a tadpole. *a*, Capillary vessel extending by means of its terminal protoplasmic filament. *b*, *c* and *d*, Protoplasmic masses or cells by which a capillary network will eventually be formed. (Arnold.)

to kill a part with its vessels by the action of sulphuric acid, the latter must have a certain concentration; a weaker solution is, however, far from innocuous, although it does not instantaneously destroy the vitality of the vessel walls. These examples will, I think, explain the drift of my thoughts, for they show that alterations in the constitution of the vessel walls, for which the term *molecular* just now appears to be the most suitable designation, are called forth by a number of influences of the most different kinds. But if such alterations occur we are justified

in asking, What effect have they upon the circulation?

"Yet however natural this question, it is impossible to answer it *a priori;* the direct observation of appropriate cases is necessary, and it will be best, with this end in view, to have recourse to express experiment. This may be carried out without any difficulty. You need only expose the vessels of a part to the air by removing its protective coverings, when, if you have selected a transparent tissue, there is nothing to hinder microscopic observation. The simplest method is to draw out the intestine of a curarized frog through a laterally placed opening in the abdominal wall, and to bring the mesentery under the microscope, after having carefully spread it out on a slide adapted to the purpose.". . . "The first thing you notice in the exposed vessels is a dilatation which occurs chiefly in the arteries, then in the veins, and least of all in the capillaries. With the dilatation which is gradually developed, but which, during the space of fifteen to twenty minutes, has usually attained considerable proportions (often exceeding twice the original diameter) there immediately sets in in the mesentery an acceleration of the blood stream, most striking again in the arteries, but very apparent in the veins and capillaries also. Yet this acceleration never lasts long; after half an hour or an hour, or sometimes after a shorter or longer interval, it invariably gives place to a decided retardation, the velocity of the stream falling more or less below the normal standard, and so continuing as long as the vessels occupy their exposed position. Such is the course of events in the mesentery experiment, in which not only the vessels of the mesentery, but their terminal ramifications in the intestine, are laid bare. In the wound of the (frog's) tongue, on the other hand, the acceleration is often altogether absent; and from the first there is associated with the dilatation a retardation of the stream, which increases as the dilatation increases.

"This stage having been reached, the vessels are seen to be all of them very wide; a multitude of capillaries which, even formerly, were hardly perceptible, can now be clearly distinguished; pulsation is usually conspicuous on into the finest ramifications of the arteries; while the flow is everywhere slower than normal, so that the individual corpuscles may easily be recognized not only in the capillaries, but also in the veins, and during diastole in the arteries. In consequence of the tardy, forward movement the corpuscles accumulate in large numbers in the capillaries, so that the latter appear redder than usual, and therefore fuller, more voluminous; yet their cross section, as just stated, is only very inconsiderably enlarged. But it is the veins rather than the capillaries that attract the notice of the observer; for slowly and gradually there is developed in them an extremely characteristic condition; the originally plasmatic zone becomes filled with innumerable colorless corpuscles. The plasmatic zone of the veins, you will remember, is always occupied by scattered colorless blood corpuscles which, owing to their globular form and low specific gravity, are driven into the periphery of the stream, and whose adhesiveness makes it difficult for them to escape from the wall once they have come into contact with it. It is obvious that this difficulty will be enhanced in proportion to the slowness of the blood stream; and thus it is not surprising that a gradual accumulation of large numbers of colorless corpuscles should take place in the peripheral zone, and here come to be comparatively motionless. For that a state of absolute rest, an actual standstill is out of the question, I need hardly mention expressly; the colorless cells of the plasmatic layer remain stationary at most for a time, they then advance a little, and perhaps make another short halt, and so on. Yet this does not lessen the striking contrast presented by the central column of red blood corpuscles, flowing on in an uninterrupted

stream of uniform velocity, and the peripheral layer of resting colorless cells; the internal surface of the vein appears paved with a single but unbroken layer of colorless corpuscles without the interposition at any time of a single red one. It is the separation of the white from the red corpuscles that gives the venous stream in these cases that characteristic appearance, anything analogous to which you will look for in vain in the other vessels. For in the capillaries, although large numbers of colorless blood corpuscles adhere to the walls, there is always an admixture of red cells, or rather these are very decidedly in the majority. Lastly, in the arteries there is seen during diastole, almost at the moment of exit of the wave, a number of colorless blood corpuscles rolling straight towards the periphery; yet these are always swept into the stream at the next systole, so that the development of a resting peripheral layer is here altogether out of the question.

"But the eye of the observer hardly has time to catch all the details of the picture before it is fettered by a very unexpected occurrence. Usually it is a vein with the typical peripheral arrangement of the white corpuscles, but sometimes a capillary, that first displays the phenomena. A pointed projection is seen in the external contour of the vessel wall; it pushes itself further outwards, increases in thickness, and the pointed projection is transformed into a colorless rounded hump; this grows longer and thicker, throws out fresh points, and gradually withdraws itself from the vessel wall, with which at last it is connected only by a long thin pedicle. Finally, this also detaches itself, and now there lies outside the vessel a colorless, faintly glittering, contractile corpuscle with a few short processes, and one long one, of the size of a white blood cell, and having one or more nuclei; in a word, a colorless blood corpuscle. While this is taking place at one spot, the same process has been carried on

in other portions of the veins and capillaries. Quite a large number of white blood cells have betaken themselves to the exterior of the vessels, and these are constantly followed by fresh ones, whose place in the peripheral layer is immediately occupied by others. Like every stage of the entire process or from the time of exposure, these phenomena may develop either rapidly or slowly: at one time the earliest emigration very quickly succeeds the pavementing; at another, an hour or more may pass without anything happening to draw the attention to the contour of a single vein or capillary. In any case the final result, after six or eight or more hours have elapsed, will be the enclosure of all the veins, small and large, of the mesentery or wound of the tongue with several layers of colorless blood corpuscles. These fence in the veins, in the interior of which the previously described conditions continue, namely, the peripheral arrangement of the colorless cells and the central unbroken flow of red blood corpuscles. Nothing analogous has occurred in connection with the arteries, their contour has remained smooth as before, nor can a solitary corpuscle, red or white, be discovered on their outer surfaces, except, of course, such as may have reached them from the neighboring veins. On the other hand, the capillaries take, as already mentioned, a very active part in the process; yet these and the capillary veins differ remarkedly from the veins proper in that not merely colorless, but red corpuscles, emigrate from them. This result is completely in harmony with the condition of the stream in these vessels, for I have already called your attention to the fact that in the veins only white corpuscles, in the capillaries both varieties, are in contact with the vessel wall, so that whether a preponderance of white or of red corpuscles passes out of a given capillary depends solely on the numerical relations of the cells accumulated in its interior.

"Keeping pace with this exodus, emigration, or, as it is also called, extravasation of corpuscular elements, there occurs an increased transudation of fluid, in consequence of which the meshes of the mesentery, or the tissues of the tongue, are infiltrated and swell. But this is not all. The extravasated colorless corpuscles distribute themselves, in proportion as their numbers increase, over a larger area, forsaking the neighborhood of the vessels from which they are derived. The tissues become more and more densely packed with them, while the red cells, which have not the power of independent locomotion, remain seated in the vicinity of their capillaries; yet these also may be carried off by the stream of transudation. Soon a moment must arrive when the products of exudation and transudation can no longer be accommodated in the tissues. They now gain the free surface of the mesentery, and should the transuded fluid coagulate, as is the rule here, the final result of the process just described will be the deposition on the mesentery, as well as on the intestine, of a fibrinous pseudo-membrane, densely packed with colorless blood corpuscles, and interspersed with isolated red cells."

Inflammation then is a process characterized chiefly by vascular changes. Its chief phenomena are vascular dilatation, slowing of the blood stream, perivascular edema, emigration and diapedesis. In situations where the blood vessels are absent, as in the cornea, the essential phenomenon is leucocytic migration. In either case the tendency is to healing or repair of the lesion.

Very many inflammations are the result of infection with bacteria (septic inflammations). In these the process is generally the same so far as the fundamental tissue and vascular changes are concerned. The following description is taken from Adami's book on "Inflammation," a book which every student will be interested to read. In it he summarizes the observations of Hohnfeldt

on abscess development through the agency of staphylococcus pyogenes aureus: "He inoculated small quantities of pure cultures of the microbe subcutaneously into rabbits. Four hours after inoculation the vessels of the region were found densely filled with corpuscles, and in them a commencing margination of the white corpuscles was discernible. Leucocytes were present within the tis-

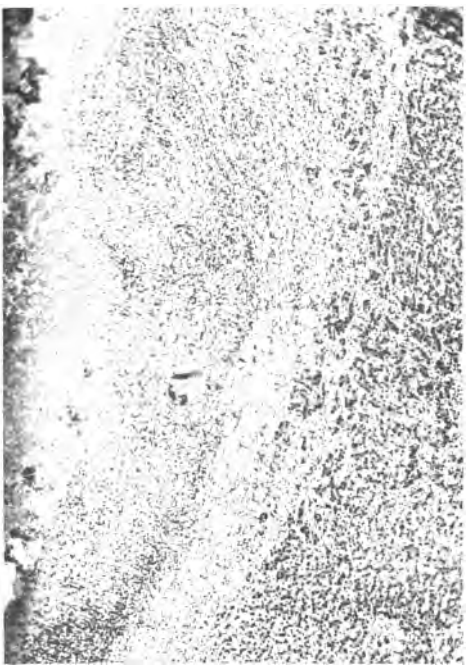

Fig. 17.- A section of an area in the liver which is the seat of a tuberculous process. In this instance the infection is in the tissue about a bile vessel. Note the giant cell.

sue in numbers greater than normal; although compared with later stages they were infrequent. They were of two kinds—the mononuclear in the majority, the polymorphonuclear in lesser numbers; both forms were congregated mainly around the line of entrance of the injecting needle. Many of the connective tissue cells were so swollen as to be rounded rather than flattened. The

injected cocci, lying in the lymph-spaces, were scattered through the tissue; in part free, in part already ingested by cells, not only by the leucocytes, but also by the connective tissue cells, the number within leucocytes being not inconsiderable. Preparations made at the end of ten hours showed the same conditions, but more distinctly. There was ample evidence of migration of the leucocytes;

Fig. 18.—A photograph of granulation about an area of chronic tuberculosis. This illustrates well why such areas have been called granulomas.

margination in the congested vessels, various stages of passage through the vascular walls, and large collections of cells in the perivascular lymph spaces; from these they spread into the spaces between the bundles of connective tissue fibrils. The cocci lay in the lymph spaces in increased numbers, and the massing of leucocytes corresponded in position to the accumulation of microbes. In

these regions the leucocytes were mainly polymorphonuclear, but in the boundary zone away from the cocci the mononuclear form predominated. At the end of twenty hours there was further accentuation of these conditions. As yet an abscess proper had not been formed, but there were enormous numbers of leucocytes and also of micrococci; the fibrillæ of connective tissue were widely separated by the collections of leucocytes, which clus-

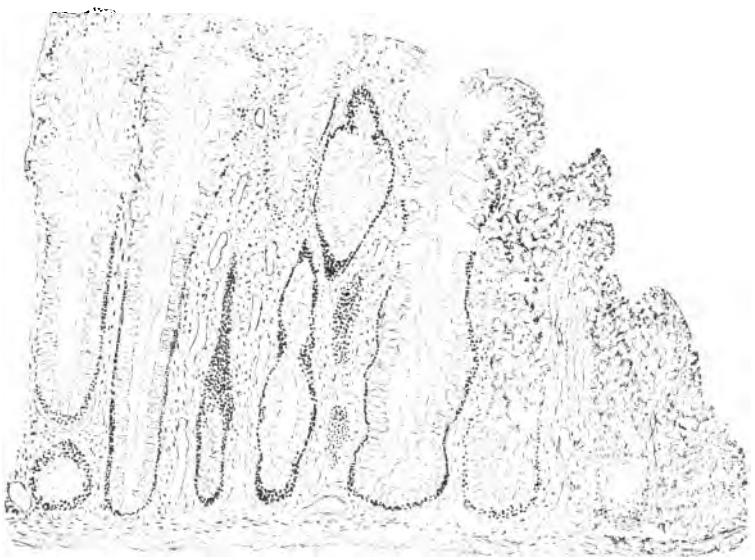

Fig. 19.—Acute catarrhal colitis. The epithelium of the tubular glands, especially near their mouths, is forming an excessive amount of mucus with destruction and exfoliation of the cells. The tubules are dilated with mucus which covers the surface. The mucosa at the right is necrotic and forms the edge of an ulcerated area. (Delafield and Prudden.)

tered round and hid the connective tissue cells. With the completion of forty-eight hours a well-defined abscess had formed, separated sharply from the surrounding healthy tissue. The center of the abscess was seen to consist of densely packed leucocytes mingled with large growths of cocci. These leucocytes were almost entirely polymorphonuclear; and in this central area the nuclei of some showed fragmentation. (Such a matrix constitutes pus.)

Neither leucocytes nor connective tissue cells showed the slightest indication of mitosis. In the central area all traces of the previous capillaries had disappeared; in the peripheral zone they were easily recognized, being fully injected; and showing a marginal disposition of their leucocytes, many of which could be seen (in osmic acid preparations) fixed in the process of migration. The major-

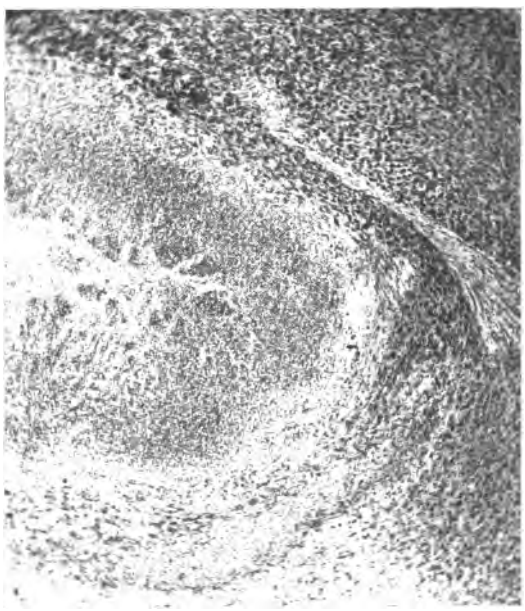

Fig. 20. An abscess of the liver. The central part is composed of leucocytes, some of them apparently living and some of them dead. There are fragmented cells and parts of cells lying in the more fluid portion of the mass. This whole central area is what is known as pus. About the abscess the liver tissue is compressed and infiltrated with leucocytes, some of them on their way into the abscess to act as scavengers (phagocytes), some of them on their way out of the abscess carrying off dead material.

ity of the cocci lay in these leucocytes. Even where the colonies of the microbes were thickest, there the majority were intracellular. Passing toward the periphery the number of cocci became smaller and smaller. At the periphery they could be seen not only to be intracellular, but also free in the lymph spaces; and Hohnfeldt, with

other observers, saw them definitely grouped within the endothelial cells of the peripheral vessels. Thus it may be noted that, at this stage, the proliferating microbes extended into the healthy tissues outside the abscess. In the center of the abscess the original tissue had wholly disappeared; nearer the periphery light streaks and bundles of the disintegrating fibrillæ could be recognized between the leucocytes. Not until the tenth day did new growth of tissue begin to show itself. During the preceding six days there had been mere breaking down of the polymorphonuclear cells, characterized by fragmentation of the nuclei and by fatty degeneration of the cell substance. But by the tenth day the periphery had begun to assume the appearance of granulation tissue; it contained numerous capillaries and new-formed connective tissue with characteristic epithelioid cells or fibroblasts possessing larger, oval, pale-staining nuclei. In these cells, as in the connective tissue cells of the surrounding tissue, the numerous steps of indirect cell division could be made out. In this granulation tissue cocci were absent and leucocytes were infrequent."

Such is the typical picture of abscess formation and the progress up to the commencement of healing. The fact should be mentioned here that, at almost any stage of this process, the bacteria may enter the blood stream and be distributed to the rest of the body. Then one of two things may happen; either the bacteria may proliferate exclusively in the blood and overwhelm the infected organism, a condition which we know as *septicemia*, or they may become located in other organs or tissues and there proliferate and produce other secondary or metastatic abscesses, a condition known as *septicopyemia*. It is also possible that the bacteria without of necessity entering the blood stream spread in an apparently unhindered and unlocalized way in the tissues, and so produce a diffuse reaction (*cellulitis; phlegmon*).

Repair and Regeneration.

If, as the result of a trauma only a few cells are damaged (as illustrated in the lesion produced by a sharp knife or a pin prick), and the edges of the wound remain in apposition or very close together, healing takes place very rapidly. There is little dead material to be removed, and a few phagocytes can do the necessary work quickly. The blood or serum which is present below the

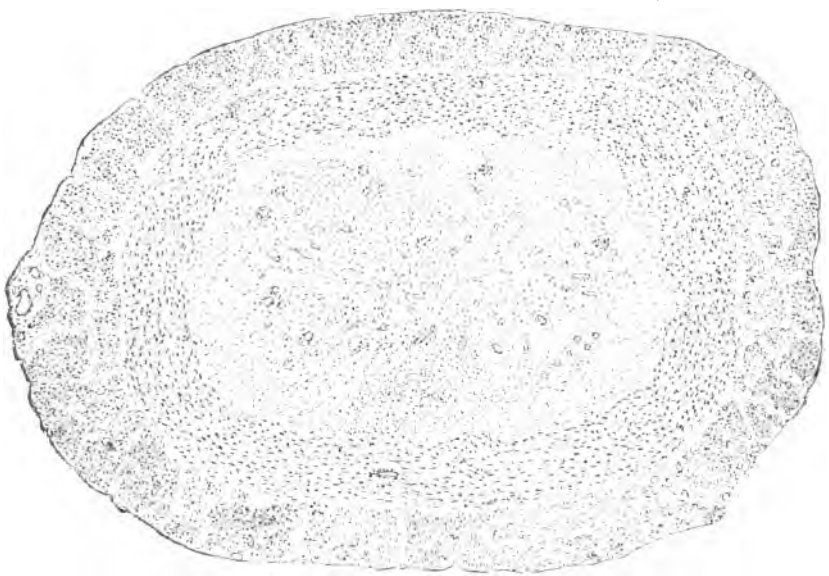

Fig. 21.—An appendix vermiformis which has been the seat of an inflammatory process. The lumen of the appendix has been filled with an exudate which instead of being absorbed has been organized. (Delafield and Prudden.)

edges of the wound coagulates and glues them together and the fibrin formed during coagulation forms a network upon which the cells for either side can be supported in their growth. The result is that the capillary loops send their sprouts across the wound: the fibroblasts, few in number, grow with the capillaries and form a permanent binding of the tissue. At the same time the epithelium of the surface grows across the wound and covers it.

At the end of a few days the healing is complete and strong. This we call "*healing by first intention,*" and it is what the surgeon strives for in approximating the edges of the wounds he makes with his sharp instruments. Tearing of tissues tends to destroy more cells and delay healing.

In *healing by second intention* or healing by granulation one of two things has happened: either the space to be filled with tissue is too wide for rapid filling with living cells, or infection has occurred. If a wound is filled with sterile blood clot, healing will occur especially by means of organization of the blood clot; if the wound or the blood clot is infected (stitch abscesses for instance) then the process of healing is analogous to that already described in the formation and healing of abscesses. Such healing results in the formation of much fibrous tissue, which tends to produce a scar and scar tissue, especially when it replaces muscle, and tends to stretch.

Fibrous tissue is the tissue with which all other tissues are apt to be replaced if healing is not rapid. Many tissues do not regenerate save only very slowly. Fibrous tissue grows rapidly and hence tends to replace the "nobler" tissues. The more highly developed a tissue is the less power it has of regeneration. Complex tissues never undergo complete regeneration. The nearest approach to it is seen in per primam healing.

In healing of wounds in bone the process is much the same as in other situations. It is only modified by the fact that the fibroblasts play a role which is supplemented by osteoblasts, which are merely modified fibroblasts. After a fracture there is a certain amount of hemorrhage which fills in the spaces between and around the broken ends of the bones. Associated with this there is exudation of cells and serum. Soon the blood clot which is formed begins to organize and the whole mass forms what is known as the callus. This callus is finally, in

part, replaced by osteoblastic tissue, and finally by bone, and is in part absorbed. Sometimes it is not replaced, but remains fibrous and then we speak of "fibrous union of bones." This is what is apt to happen in old persons, in persons whose bones are not well "set" or approximated, and in those in whom the bones are not kept solidly in place during healing.

Types of Inflammation.

Inflammations are classified according to the time during which they have existed, or according to the morphologic characters of the exudates. For instance they are called *acute* if they appear and develop within a very short time or last but a short time; they are called *chronic* if they develop slowly or last a long time. One remembers the acute coryzas which appear almost in a minute, last a few days and disappear, or the acute tonsillitis which acts in the same way. A boil is an acute inflammation. One also remembers the "colds" that last all winter; the bronchitis of old people, which lasts for years as is shown by the "chronic" cough, and the pulmonary tuberculosis with which some individuals live for years. On the other hand one recalls the terms "membranous croup" (which we now know is diphtheria), which referred to the membrane found in the larynx. A membrane is an exudate formed almost purely of fibrin, with sometimes a few leucocytes. An abscess is a purulent form of inflammation, for purulent refers to pus. A serous inflammation is characterized by the predominance of serum; a hemorrhagic inflammation, by the presence of numbers of blood cells. A catarrhal inflammation is one whose exudate contains much mucus (a mucous inflammation). Also there are serofibrinous inflammations; seropurulent; fibropurulent, and other inflammations,—terms which explain themselves. Suppuration is a term which

means the same thing as purulent. Any of these forms of inflammations may be acute or chronic.

An abscess is a localized purulent inflammation in a tissue. An ulcer is a localized purulent inflammation upon a surface. A sinus is a localized inflammatory tract connecting two surfaces.

The types of inflammation depend upon the nature of the tissue affected; upon the nature of the irritant; and upon the intensity and duration of the irritant action. For instance, the skin of the hands is less easily affected by heat and cold than the skin of the body. Dilute carbolic acid placed upon the surface of the body does no damage, while strong carbolic acid will produce local death of cells. Heat of great intensity will do no damage if it be applied momentarily to the skin, but if a moderately hot object be left in contact with the skin for a certain length of time it may produce a burn. Under certain conditions a hot water bottle placed upon a patient will burn, while under other conditions of health and resistance it would do no damage. So, there enters into the question the problem of individual resistance. It is this relationship that accounts for the fact that certain bacteria produce no effects in one person and disease in another.

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CHAPTER VIII.

TUMORS.

In the old sense of the word the expression tumor was applied to swellings of any sort (hematoma, tuberculoma, syphiloma). Usage in that sense is no longer proper and now the word is applied to certain types of hyperplastic tissue growths, which are more or less autonomous. The term neoplasm is still better, because it is a more concise

Fig. 22.—An epithelioma of the hand.

one and implies, through usage, independence and hyperplasia.

"A tumor proper," says C. P. White, "is a mass of cells, tissues, or organs resembling those normally present, but arranged atypically. It grows at the expense of the organism without at the same time subserving any useful function."

The ordinary tumors which are seen in the wards of hospitals belong to a group known as the *blastomas*. They are derived from but a single tissue in each instance and according to the tissue from which they originate their names arise. For instance a tumor growing from

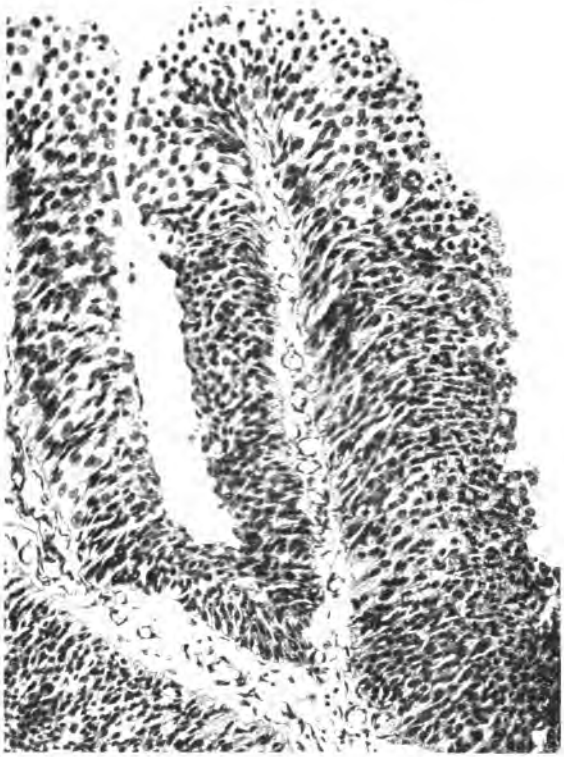

Fig. 23.—Mucous papilloma of bladder, composed of long slender branching processes with delicate vascular core covered by proliferated transitional epithelium—the so-called *Villous Papilloma.* (×200.)

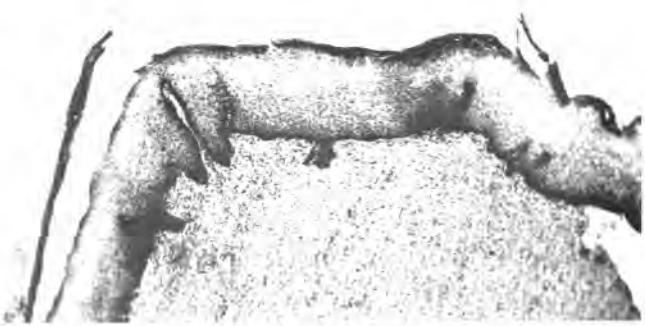

Fig. 24.—Photograph of a section of a bit of skin sent to the laboratory because there was a suspicion of malignancy in the case. There is nothing malignant to be seen, but the section illustrates the earliest histologic tendency in the direction of invasive proliferation of the subcutaneous tissues by the epithelium. Note the small abscess cavities.

epithelium is called an epithelioma; from fibrous tissue a fibroma; from bone, an osteoma, etc. There are also a certain group of tumors which arise from more than one tissue and these are the teratoblastomas or ordinary

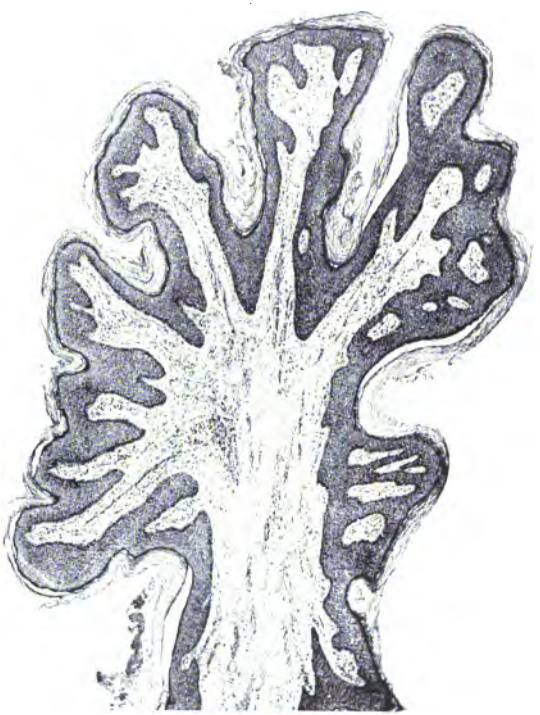

Fig. 25.—Squamous papilloma, showing thickened skin epithelium, covering a branching vascular connective tissue core. (x38.)

mixed tumors which are frequently encountered in the parotid region of the body.

Depending upon the course which the growth of a tumor takes we speak of benign and malignant neoplasms. The former is one which is not incompatible with health; the latter is a menace to existence.

The following table will indicate the commoner terminology as well as the origin of the tumors:

SOURCES	BENIGN	MALIGNANT
Epithelium (skin)	Benign epithelioma	Epithelioma; (Skin cancers)
	Papilloma (warts, corns)	
Epithelium (glands)	Adenoma	Carcinoma (Adenocarcinoma)
Mammary gland		
Epithelium of intestine, liver, pancreas, etc.	Adenoma	Carcinoma (Adenocarcinoma)
	Papilloma; Polyps.	Carcinoma
Connective tissue	.....	Sarcoma
Fibrous tissue	Fibroma	Fibrosarcoma
Fatty tissue	Lipoma	Liposarcoma
Bone tissue	Osteoma	Osteosarcoma
Cartilage	Chondroma	Chondrosarcoma
Muscle	Myoma	Myosarcoma
Nervous system		
Neuroglia	Glioma	Gliosarcoma
Endothelium	Endothelioma	Endothelioma
Blood vessels	Angioma	Angiosarcoma

The main differences between benign and malignant tumors is shown in the following table:

BENIGN.	MALIGNANT.
Slow growing	Rapidly growing
Circumscribed (Encapsulated)	Not encapsulated (infiltrating)
Do not metastasize	Metastasize
Do not interfere with health	Produce evident interference with health by pressure upon other organs, by producing anemia, cachexia, etc.

Sarcomas are more frequent in young individuals.

Carcinomas are more frequent in older individuals.

Tumors are apt to be most frequent at places in the body where there is continued irritation. Such irritation may be due to bacteria, to toxins, to other chemical irritants, or to mechanical influences. Just why tumors start to grow no one knows.

Fig. 26. Epithelioma of the lip.

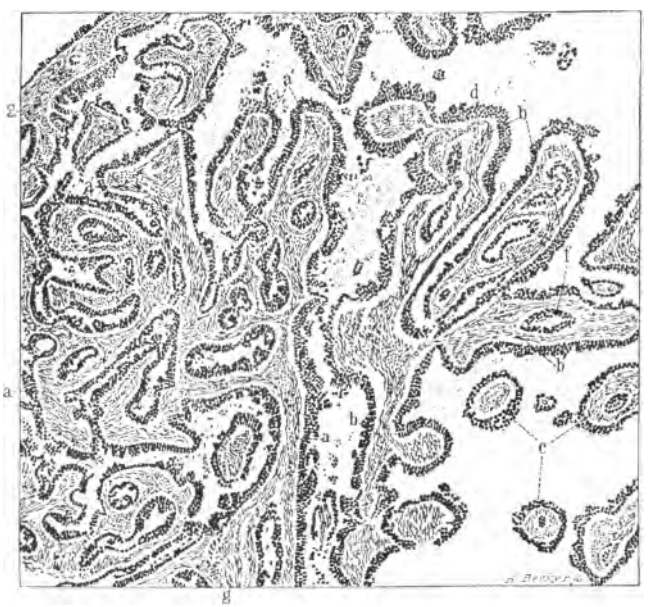

Fig. 27. —Adenocarcinoma of the cervix uteri. Almost the entire field is made up of the main trunks *a* and *b*, which send off many branches, *a'* and *b'*. *c* indicates cross sections of terminal outgrowths. The stroma *g* consists of elongate cells with spindle-shaped nuclei. Covering the outer surfaces of the main and terminal branches are layers of epithelium, a single layer at *c*, several at *a*. (Cullen.)

Fig. 28.—Sarcoma.

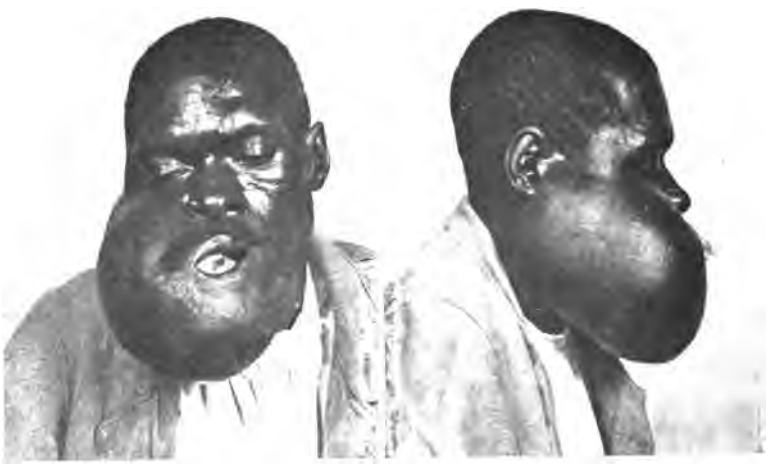

Fig. 29. Fig. 30.

Figs. 29 and 30.—Sarcoma.

Tumors spread in two ways by infiltration, i. e., by direct growth into other tissues, which are destroyed; and by metastasis either by the lymphatic vessels or the blood vessels. Sarcomas are more apt to follow the blood vessels; carcinomas to follow the lymphatics.

No one knows what the cause of tumors is, and therefore no one knows how to prevent them, or in many cases,

Fig. 31.—Fibrolipoma.

Fig. 32.—Small polyp of the mucous membrane of the small intestine. (Delafield and Prudden.)

to cure them. All that is certain, therefore, is that the most certain cure is to remove them completely. With benign tumors this is usually easy. With malignant ones it becomes increasingly difficult, the longer the tumor has been allowed to persist, though it is true that in a few instances spontaneous healing has occurred. There is some hope at the present time that x-rays and radium emanations may have a beneficial influence in the treatment of tumors.

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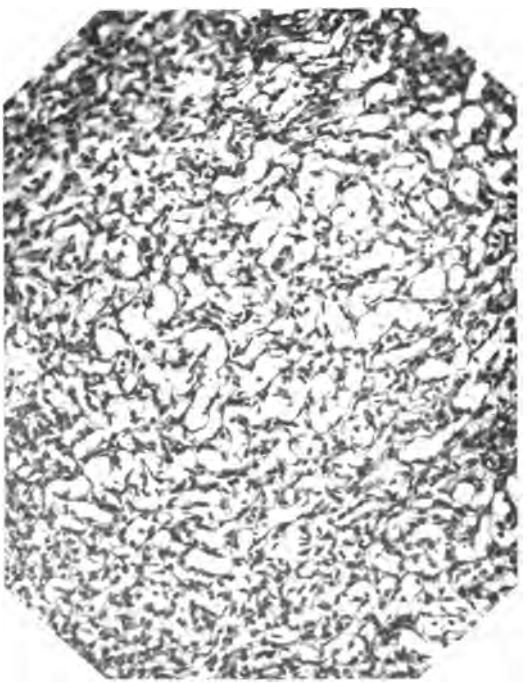

Fig. 33. —An angioma, i. e., a tumor composed entirely of blood vessels. There are two sorts of angiomas; one composed as in this case of blood capillaries (hemangioma); the other composed of lymphatic vessels (lymphangioma).

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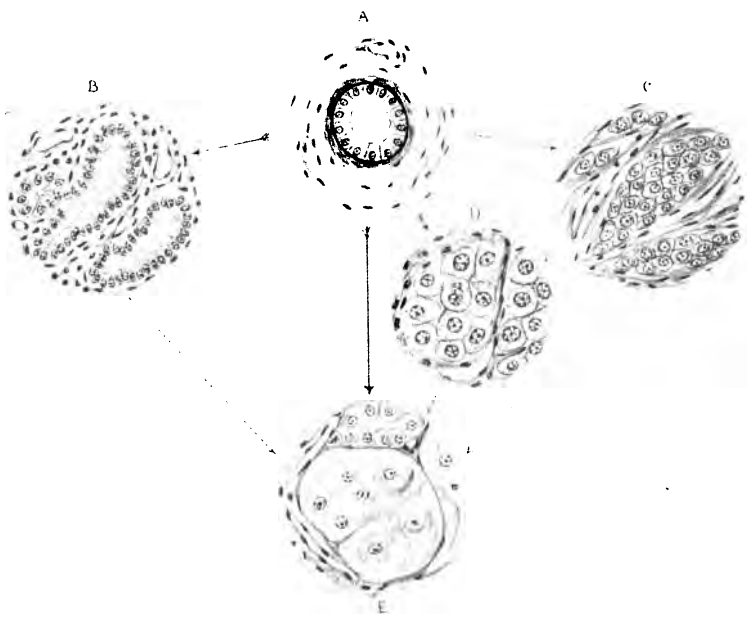

Fig. 34.—Schematic representation of the varieties of cancer which may arise from glandular epithelium. (After Beattie and Dickson.)

A. Transverse section of Normal Gland Acinus consisting of regular epithelium upon a basement membrane, surrounded by a connective tissue stroma containing nutrient vessels. This may give rise to any of the following types of new growth.

B. Malignant Adenoma, with irregularity in shape of acini, the lumen of which persists. Absence of basement membrane. Irritation giving rise to proliferative overgrowth, etc., of stroma.

C. Scirrhus or Hard Cancer, in which solid clumps of cells are formed, and give rise to dense fibrous tissue overgrowth.

D. Encephaloid or Soft Cancer, which may arise directly, or may supervene upon the harder variety, the two resembling one another in being composed of solid clumps of cells.

E. Colloid Cancer, which may arise directly from the normal gland type, or may supervene upon any of the other forms.

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PART II—SYSTEMIC PATHOLOGY

CHAPTER IX.

THE CARDIOVASCULAR SYSTEM.

The Blood.

Normally the body contains a certain average amount of blood, including certain fairly definite properties of fluid (plasma), and the cells (red cells, leucocytes and platelets). In disease these proportions vary. According to the type of variation we speak of *general* hyperemia or *general* anemia. Also under normal circumstances the distribution of the blood in the body remains constant. In disease the distribution varies and we speak of *local* hyperemia or *local* anemia, as the case may be.

Depending upon the constituent of the blood which is increased, there are certain terms in use. For instance, a general increase in the total blood is spoken of as plethora; increase of the fluid constituents, as hydremia; of the red elements, as polycythemia; of the leucocytes, as leukemia. The term anemia covers a large field but most frequently has reference to diminuation of the hemoglobin concentration of the blood. Decrease of the leucocytes is called leucopenia. Total decrease of blood we call oligemia; of fluids only, anhydremia.

Hyperemia.

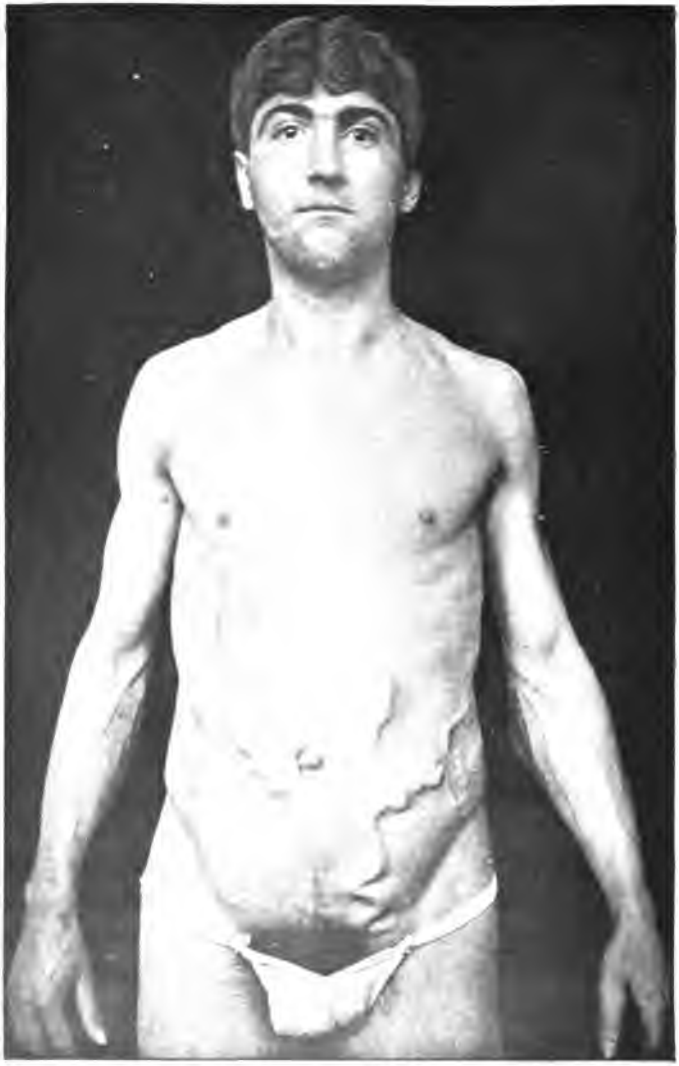
Hyperemia may be, as we have indicated, general or local, arterial or venous. Normally there is in the human body about one-twentieth its weight of blood. In infants

THE BLOOD CORPUSCLES. (After McFarland.)

- **Corpuscles**
  - Absolutely increased — *polycythemia.*
  - Absolutely decreased — *oligocythemia*
- Erythrocytes measure 7.5μ, 5,000,000 per c.mm.
  - Deficient—anemia.
  - Increased—*Polycythemia.*
  - Peculiar
    - In size
      - Abnormally small—Microcytes—*Pernicious anemia.*
      - Abnormally large Macrocytes and megaloblasts—*Pernicious anemia.*
    - In structure—Nucleated—Megaloblasts—*Pernicious anemia.*
    - In shape—Poikilocytes—*Pernicious anemia.*
    - In color
      - Absolute deficiency of hemoglobin—*Chlorosis.*
      - Absolute increase of hemoglobin—*Pernicious anemia.*
    - In staining Polychromatophilia—*Pernicious anemia.*
- Leucocytes measure 7 to 12μ, 7,500 per c.mm.
  - Deficient—*Leucopenia.*
  - Increased—*Leucocytosis.*
    - Cells normal to the blood.
      - Polymorphonuclear
        - Physiologic—post prandial.
        - Pathologic—infection.
      - Lymphocytes *Lymphocytosis.*
        - Physiologic—infancy.
        - Pathologic—*Lymphatic leucemia.*
      - Eosinophiles *Eosinophilia*
        - Physiologic—infancy.
        - Pathologic
          - Infection—Helminthiasis
          - Trichiasis.
          - Uncinariasis.
    - Cells abnormal in the blood—Myelocytes—*myelogenous leucemia.*

there is more, in old persons less. This weight or volume of blood can be increased temporarily by injecting fluids into the body, particularly by the intravenous route, but the fluid so injected, unless it be held by a colloid, as, for instance, gelatine, is very rapidly eliminated. Nevertheless under certain abnormal circumstances the whole volume of blood increases, or in other cases one of its constituents becomes augmented. Plethora is uniformly associated with either polycythemia or with one or another type of anemia.

In local hyperemias, however, things are different. When the hyperemia (or congestion) is the result of arterial activity, when it is produced by the presence of arterial blood, we speak of active congestion; when it results from decreased drainage of the blood through the venous channels, we call it passive congestion. When for any reason the arteries or arterioles are dilated, whether by nervous impulses, or by chemical causes, more arterial blood rushes into the affected part. This we call arterial (or active) hyperemia, or congestion. If, on the other hand, without any participation on the part of the arteries, blood is prevented from leaving an organ, we call it venous (or passive) hyperemia or congestion. Active (arterial) hyperemia is the cause of the very well known blush or flush. It is also the phenomenon which accounts for the increase of blood in a functionally active organ, like a muscle, or the stomach. It is the cause of the redness that appears during inflammation. Passive congestion, on the other hand, results from increased venous pressure and may be cause by blocking of a vein from within or from without. When the heart is so damaged that blood is prevented from entering it at a normal rate because of disease of the tricuspid valve, the liver becomes the seat of a passive congestion. When the mitral valve is damaged so that the blood coming from the lungs cannot pass through it rapidly enough, the lungs become



Abdominal dropsy in a case of chronic tuberculosis of typhoid origin.
(Osler.)

passively congested. The pressure of fluid in the pleural cavities may so affect the circulation of blood that the circulation from the right to the left heart is impeded and the organs of the abdominal cavity become passively

congested. Air in the pleural cavity, or tumor growths, may produce the same effects, and very similar ones follow the accumulation of large amounts of fluid in the pericardial cavity.

The arterial hyperemias are as a rule transient ones, and are in physiologic circumstances associated with transient increase of function. When a muscle is exercised, more blood is carried to it, and with the blood more food. Functional activity and increased food lead to growth. The venous hyperemias, on the contrary, tend to be more permanent—chronic, we call them, and these chronic passive congestions lead to the opposite changes to those which follow arterial hyperemias. The damming back of venous blood prevents the arterial blood reaching the parts. The venous blood, which is poor in oxygen and other foods, accumulates and the functional cells of the affected tissue tend to undergo atrophy, while the fibrous tissue becomes richer. In the liver, for instance, the cells affected by the passive congestion do not receive oxygen enough and commence to degenerate. More than a normal amount of fat appears in them; they shrivel, become atrophic and disappear. At the same time the fibrous tissue is accentuated by loss of liver cells and also undergoes increase and the organ becomes fibrous-cirrhotic. And also because the venous blood (some of it) cannot get out of the tissue, the blood cells die, the pigment is set free and stains the tissue. The gross result is that the liver takes on an appearance that resembles the cut surface of a nutmeg and the organ is known as the nutmeg liver. Much the same thing happens in the lungs. They become fibrous—indurated, and pigmented, but some of the pigment and some of the blood passes into the air spaces and is coughed up. When free blood is present the sputum is tinged with red; when only pigment is present, the sputum is "rusty."

Anemia.

Anemia, like hyperemia, may be general or local. General anemia may be caused by large single losses of blood as from large hemorrhages, or by many small losses. Severe grades of anemia may be caused by the small frequent hemorrhages from hemorrhoids. More frequently, however, severe anemia is the result of intoxication with substances which cause destruction of the red blood cells. The so-called pernicious anemias, or primary anemias, are almost certainly of infectious origin, although there is the possibility that some forms may be the result of wearing out of the blood forming tissue of the body. The primary anemias are those whose causes we have not discovered. The secondary anemias are those the causes of which are known.

Local anemias are as a rule the result of interference with the blood flow. Such interference may take place within the vessels or by pressure from without. One of the best examples is a bed sore which is the direct effect of extravascular pressure. When the blood supply of a part is cut off, that part dies. In the case of the bed sore (decubitus) the area is usually circular, and corresponds to the pressure. In the case of gangrene of a leg produced as a rule by intravascular disturbances, all the tissues, whose blood supply is cut off, die.

Sometimes it happens that the blood supply of a part is interrupted for but a short time. In most instances only temporary effects are produced. In other cases the interference is permanent but because of collateral pathways blood still reaches the part in sufficient amounts to prevent death or necrosis. As time goes on these collaterals become more and more sufficient until they are completely able to satisfy the needs of the tissues. It also is true that sometimes the collaterals are sufficient provided the blood supply is not shut off too suddenly. If blockage occurs slowly enough, the collaterals may ac-

commodate themselves whereas if the main current is suddenly shut off they are not sufficient. It therefore happens that the effects of a local anemia will vary with the rate of its production and the degree of its completeness.

Edema.

When we speak of edema we mean a condition which results from the presence of too much water in the tissues. Hence the term *hydrops*. It is a symptom which is associated with kidney disease, heart disease, lung disease, and general anemias. It is encountered during pregnancy, during the latter part of which the feet and legs often swell. It appears in the hands and fingers after severe and unaccustomed manual exercise, or even after long walks. The palms swell after catching a baseball—especially early in the season, or after rowing a boat. Moreover swelling is a symptom of inflammation. Under these circumstances the water is held in the cells and tissues of the body. When it is general, we speak of *anasarca* or general dropsy; otherwise it is known as edema. Sometimes fluid appears in the cavities of the body. When the abdominal cavity is affected we speak of *ascites*. In other cases we speak of pleural or pericardial effusions, or of hydrothorax, or hydropericardium, if the pleural or pericardial cavities are involved; of hydrocephalus, if the ventricles of the brain are affected.

Edema is the result of the presence of too little oxygen in the tissues. If we give an animal a poison which reduces oxidation in the body—which makes it impossible for the tissues to use oxygen—and which at the same time will not cause the death of the animal or tissue, the tissues swell. If we interfere with the blood stream so that the blood current is slowed and too little oxygen reaches the tissues, they swell. If we decrease that part of the blood which carries oxygen to a point where there is not enough to carry a sufficient amount of oxygen to the tis-

sues, they swell. In pregnancy the fetus *in utero* presses upon the great veins which supply the legs of the mother with blood. The blood flow is decreased and the feet and legs become swollen,—"dropsical." Tight garters will do the same thing and produce the same result. In severe anemia, in chlorosis or pernicious anemia there is not enough hemoglobin, or not enough red blood cells, or both, to carry sufficient oxygen to the tissues, and the feet and legs swell—become puffy, so that the shoes are too tight. In heart disease when the blood does not circulate rapidly enough through the lungs, especially when the arterial blood flow is interfered with, the lungs become edematous.

The reason seems to be this: when the substance of the tissues (the protoplasm) is broken down to furnish energy, acids are produced. We know, for instance, that during muscular activity, lactic acid is formed in the muscles. If the blood supply is good, enough oxygen is furnished to oxidize the lactic acid and split it until the acid part is represented by carbonic acid which is absorbed by the blood and excreted as carbon dioxide. If not enough oxygen is present, then part at least of the lactic acid remains as such. It has been found that anything in the nature of protoplasm,—gelatin, fibrin, egg albumen—takes up or absorbs water when it is placed in very dilute acids. So it happens that when not enough oxygen is carried to the tissues by the blood, the acids accumulate and the tissues absorb water from the blood, and swell. The swelling we call edema.

Thrombosis and Embolism.

Local anemia is very frequently the result of the blocking of blood vessels from within. Such blocking may occur as the result of thrombosis or embolism.

Thombosis is the process which results in the forma-

tion of a clot within a blood vessel *during life*. It may be the result of one or both of two factors.

1. *Injury to the vessel wall by toxins or other poisons, or by traumata.* When a vessel wall, especially the intimal cells, are injured, a substance called fibrin ferment is set free, which acts upon the blood and causes it to clot. The process of clotting begins in the immediate region of the cellular damage and so the clot remains adherent to the wall. It then proceeds to enlarge by progressive clotting until the lumen of the vessel is filled.

2. *Changes in the constitution of the blood itself.* Certain substances cause the cells of the blood to break up or to change the physical character of the blood, and so make it more easily able to clot. From the cells of the blood itself fibrin ferment may be set free and then, particularly if the blood is more viscid than usual, or is flowing more slowly, it may form a clot.

In either case a *thrombus* is formed.

The result, thrombosis, is of course local anemia beyond the thrombus, and if this anemia is complete, then local death or necrosis follows. If the trombus is in an artery of an organ like the kidney or lungs, the death is as a rule more rapid, and also the area that undergoes death has a tendency to be wedge-shaped, with the apex of the wedge at the thrombus. If the thrombus is in a vein, the tissue death is apt to be slower though the area is still wedge-shaped. In either case we speak of infarction. An infarct is a wedge-shaped (as a rule) area of complete local anemia in an organ and is caused by sudden interruption of the blood supply.

It not infrequently happens that a thrombus is formed within a vessel which supplies a tissue whose collateral circulation is sufficient to prevent death. Sometimes, however, from such a thrombus a piece breaks off and proceeds in the blood stream until finally it reaches another smaller vessel which it plugs. Such a free bit of

thrombus is called an *embolus*. All emboli are, however, not formed in this manner. A clump of bacteria, a bubble of air, a group of fat cells from the medulla of a fractured bone, a group of tumor cells, or a few placental cells, may be set free in the blood stream and produce embolism. An embolus is a foreign body which blocks completely or incompletely, from within, a blood vessel. The commonest examples of emboli are fragments of valvular cardiac vegetations which are broken off and are carried to the coronary arteries or brain, where they produce sudden death; or to the lungs, kidney or spleen where they produce infarcts. Infarcts may be produced by thrombi or emboli.

The Heart.

The heart is a series of chambers that have developed by dilation of a certain part of the vascular system. Its walls are fibromuscular, and its chambers are separated by valves which are merely reduplications of the endocardium. The movements of the heart are influenced by a conducting mechanism which is composed of muscle fibers of an embryonic type, and by a system of nerves belonging to the vago-sympathetic system. The nervous mechanism modifies the contractions of the muscles by producing changes which result in increased or decreased irritability of the myocardium.

The chambers of the heart serve as containers of blood; the muscles act in moving the blood; and the valves serve to direct the flow of the blood.

Pathologic changes in the heart are the results of processes which affect the muscles, the valves, the conduction system or the nervous system.

Leaving out of consideration the developmental defects, we may say that the conditions of the chambers of the heart are the results of (1) the amount of blood the heart *must receive*, and this depends upon the conditions

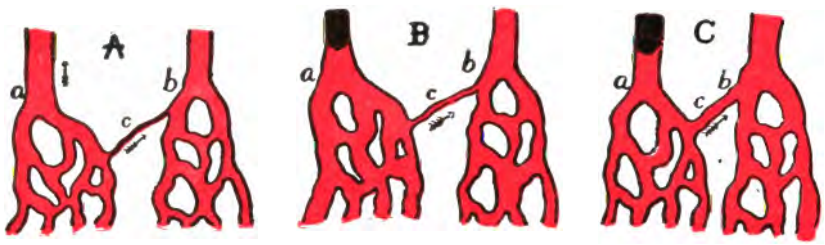


FIG. 36.—DIAGRAM ILLUSTRATING THE ESTABLISHMENT OF COLLATERAL CIRCULATION IN OBSTRUCTION OF A VEIN. (AFTER RIBBERT, FROM DELAFIELD AND PRUDDEN.)

The veins *a* and *b* at *A* are connected by a slender trunk, *c*. If *a* in *B* is occluded, as by a thrombus, the blood cannot all pass out of the territory drained by *a*, so that the vessels here are dilated—congestion. If, however, the small anastomosing trunk widens as at *c*, the congestion is relieved by the conveyance away of the blood through the vein *b*

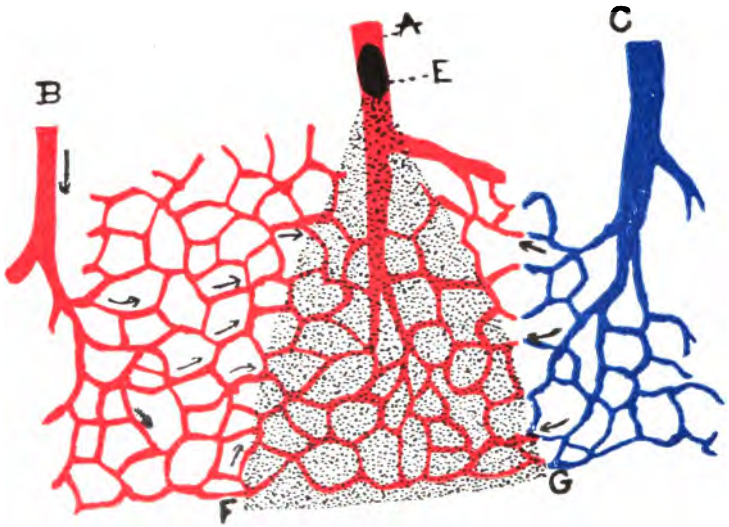


FIG. 37.—DIAGRAM ILLUSTRATING THE FORMATION OF A HEMORRHAGIC INFARCT. (AFTER RIBBERT, FROM DELAFIELD AND PRUDDEN.)

The artery, *A*, plugged by an embolus or thrombus. *E*, is a terminal artery, but it has abundant capillary anastomoses, so that while the territory deprived of blood is not sufficiently nourished and its tissues die; but from the abundant capillary anastomoses from the artery *B*, and from the vein *C*, a certain amount of blood enters the infarct area, which thus becomes hemorrhagic.

existing in the peripheral vessels, and in the blood itself (caliber of the vessels, elasticity, viscosity, resistance), and upon the condition of the valves (efficiency); and (2) upon the amount of blood they *can contain* and this depends upon the condition of the musculature.

The musculature of the heart is influenced by but two sorts of influences, i. e., mechanical and chemical, if we class nutritional disturbances as chemical, as we should.

We may properly say, then, that the musculature of the heart is modified by (1) the mechanical conditions under which it acts, which means, the work it has to do, and (2) the chemical conditions under which it acts. A heart doing a normal amount of work, that is one which is working within physiologic limits, has, other things being equal, a normal musculature. The walls of such a heart are of characteristic thickness and structure. A heart doing increased work either because of increased blood or increased work either because of increased blood or increased arterial pressure, however, behaves differently. Provided the food supply is sufficient it undergoes hypertrophy, as we say. The walls become thicker, the muscle fibers become larger and more numerous, while the cavities remain of normal relative size. But if the supply of food is not sufficient to meet the increased demands, the compensatory hypertrophy is not as marked and the cavities become larger, both relatively and absolutely. On the other hand, if the amount of work accomplished is small in amount, or if the food supply is but moderately insufficient, as is true in cases of undernutrition, in cachexia, etc., then atrophy results, and atrophy of the myocardium is apt to be accompanied by at least a moderate degree of dilatation. We may consider that we are dealing with work, increased, overwork, and lack of work in these cases. It is only when a heart is overworked that dilatation of clinical importance occurs, that is, only when the food supply is insufficient

to meet the demand of increased activity. In such cases we are dealing with muscular fatigue, with the accumulation of the chemical products of metabolism which cannot be removed rapidly enough to allow normal metabolism to proceed. Tone is lost, the muscles do not contract in a normal manner, and the cavities of the heart become larger and are less promptly and completely emptied. The chemical cardiac intoxications, such as we find in the anemias, and those produced by toxins, and poisons of other sorts, produce similar changes except that the pure work element, hypertrophy, is absent, for the reason that in these the active agents do not act as stimulants of the muscle, do not increase the work of the muscle, but act from the first by decreasing the ability to do work, and so they bring about from the start protoplasmic changes which are found only in cases of chronic overwork. If the substances acting upon the muscle are in dilute solution the changes are slow, and progression occurs from edema to fatty degeneration, atrophy, and necrosis. If the solutions are concentrated the graduations are absent. In pernicious anemia, the heart muscle is cloudy and fatty; in sudden local anemia, as in infarction, the muscle undergoes necrosis. In certain intoxications, diphtheria for instance, the heart may do very well provided no burden is thrown upon it. But place a sudden strain upon it, even that due to sitting up in bed, and what was normal work becomes overwork, because of the damaged muscle and its inability to use the materials present in the blood. *Overwork depends, therefore, on the condition of the muscle at the time the strain is put upon it.*

When a heart becomes tired out so that it no longer does its work easily, it undergoes degeneration—usually fatty degeneration. Also at the same time some of the fibers disappear and their place is taken by adipose or fat tissue or fibrous tissue. In the one case we speak of

a fatty heart, in the other of fibrous myocarditis which is often a misnomer for myocardial (or cardiac) fibrosis. But fibrous tissue may be increased in the heart as a result of inflammation, and then we may properly speak of myocarditis. Under these conditions, bacteria gain access to the myocardium and by their growth and activity kill, or cause to degenerate, the muscle fibers. Also, at the same time, exudation occurs between the muscle fibers. According to the character of the exudate, we speak of a suppurative myocarditis or hemorrhagic serous myocarditis. Usually we speak merely of an acute interstitial myocarditis. As the inflammatory lesions heal, fibrous tissue is produced and so the healed heart will have scars in it just as any other organ may have, but since during the inflammation some muscle has been destroyed, and since muscular tissue does not regenerate easily, the heart is weaker than a normal one.

Strain and infection may also affect the heart valves. Of the two processes the second is by far the more important. The bacteria which cause the infection may lodge upon the valves from the general circulation or may reach the interior of the valves by way of the small vessels which supply them. Since the latter method is more frequent and since the valvular vessels are more numerous in infants and young persons, it follows that acute valvular endocarditis is more frequent in young people and that the "valvular heart disease" of adults is more apt to be chronic.

When bacteria arrive upon or in a valve, the cells of the endocardium are sooner or later damaged and from them fibrin ferment is set free. Then, just as happens in a blood vessel, a thrombus is formed, and is usually called a *vegetation*. Hence we speak of vegetative endocarditis. The things which may happen to such vegetations are the same things which may happen to any thrombus: it may be organized; it may soften and rup-

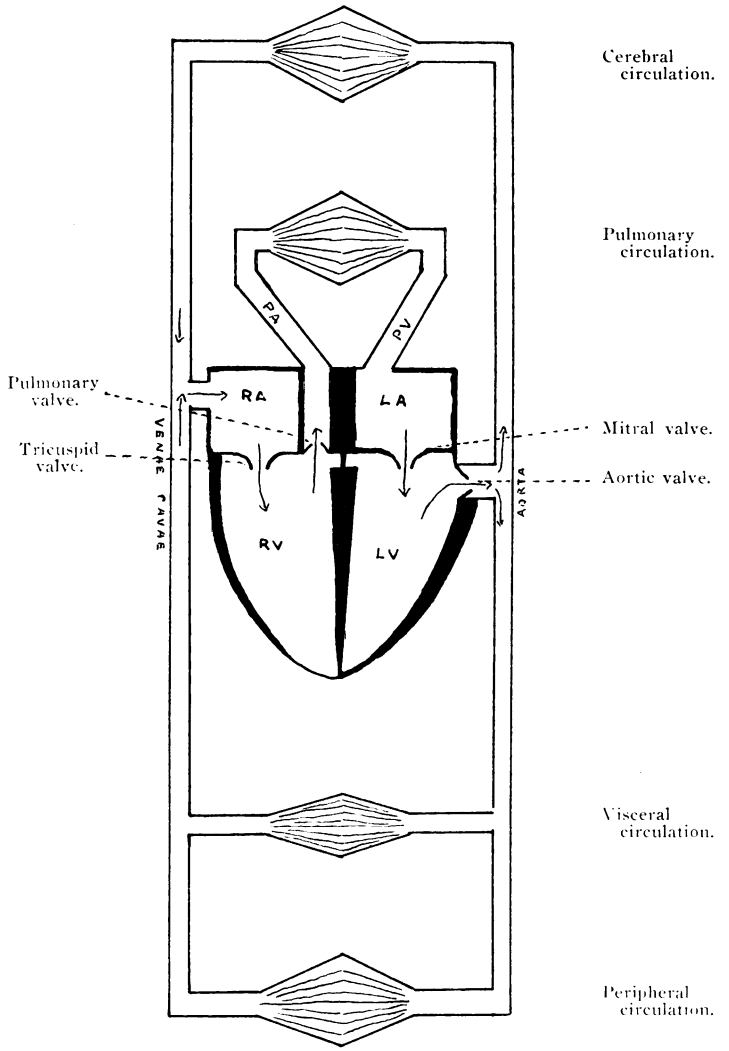


Fig. 38. – A schematic representation of the general circulation of the body. The blood leaves the left ventricle (*LV*) and enters the aorta through which it passes to the visceral and peripheral vessels to supply the abdominal organs and the limbs. It leaves the aorta and through the carotids and vertebrals supplies the brain. After passing through the various organs it is collected into the two cavæ and is returned to the heart which it enters through the right auricle (*RA*). From there it passes to the right ventricle (*RV*). From the right ventricle it is carried to the lungs by the pulmonary artery (*PA*), and it then reaches the left auricle (*LA*) through the pulmonary veins (*PV*). The pulmonary vein carries arterial blood. Suppose the mitral valve is so affected by disease that it is no longer able to prevent the blood from being forced back into the left auricle during ventricular systole (insufficiency), at every beat of the heart some of the blood which should be sent into the aorta is pushed back into the auricle and eventually into the lungs. The lungs become the seat of a "passive congestion." Eventually the back pressure effects the right side of the heart also so that the right chambers become dilated and after a time the tricuspid valve becomes unable to prevent reflux of blood (insufficiency). Then, of course, the liver and other viscera will become passively congested. If there are clots or growths (vegetations) upon the mitral valve, as in rheumatic fever, and one or more of these are broken off and become free in the blood stream, they will be carried with the blood until they become caught in some small blood vessel (artery or arteriole) which will be plugged (infarction).

ture or remain cystic; or it may be infected and break down. When the last thing happens we speak of an ulcerative (or malignant) endocarditis. Bits of the infected material carried away in the blood stream, cause infected infarcts in other organs—embolic infarcts, they are often called. If the bits of vegetations are not infected they form bland emboli and cause infarcts which are not infected. When organization of a vegetation oc-

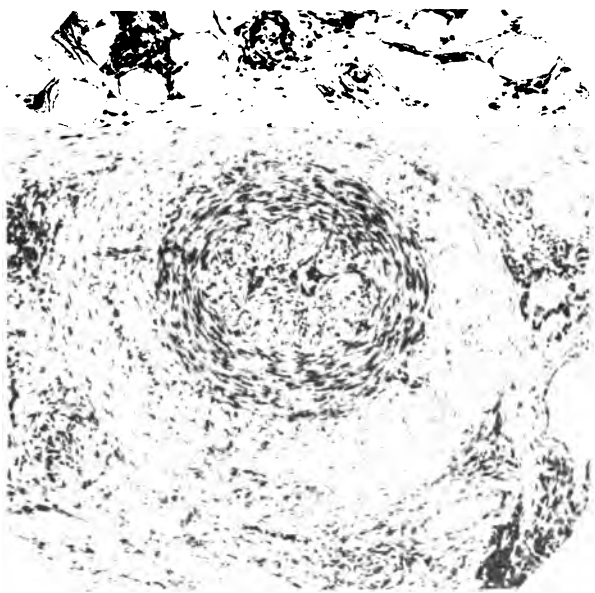


Fig. 39. Section of a blood vessel which is the seat of an obliterating endarteritis. The intima of the vessel has undergone hyperplasia to the point of almost complete closure. Such a process in the vessels (arteries) of a limb leads to death of the limb (gangrene). This section was taken from the tissues of the hand from a case of Raynaud's disease.

curs, the number of capillaries in it is increased, and so as it heals there is increased opportunity for a second infection when bacteria are present in the blood. This accounts for the fact that a person who has had an acute endocarditis, is apt to have new attacks of the same disease. If reinfection does not occur, then the valves come to have more than normal fibrous tissue in them

which makes them rigid, and as it contracts, pulls them out of shape so that the valve no longer holds the blood—is no longer competent. It produces valvular *insufficiency* or *incompetency*. Later, when the contraction has gone so far as to obstruct the flow of blood, we have produced a valvular *stenosis*.

When blood is hindered in passing through the heart it tends to be dammed back into the organs behind the valve. For instance, if the mitral valve is stenotic, then the left auricle is apt to be dilated; and the lungs will be the seat of a passive congestion, and also because the left auricle will do more work in pushing the blood past the mitral valve, it will undergo hypertrophy. The series of events applies in the case of each valve. When incompetency of a valve occurs much the same things occur. If the aortic valve is incompetent at each systole, some blood flows back to the heart from the aorta. The left ventricle consequently has more work to do, and this it meets by hypertrophy. Then it becomes fatigued in the long run and undergoes dilatation. Still later, the mitral becomes incompetent because of the ventricular dilation and then the series of changes occurs in the left auricle—and so on.

The Blood Vessels.

The blood vessels are the organs through which food (including oxygen) is carried to the various parts of the body. They are elastic tubes composed of layers of muscular, elastic, and white fibrous tissue, and are lined with endothelium. The smaller vessels, the capillaries, are composed only of an endothelial membrane. So far as they can be separated from the blood itself, they are functionally important mainly because of their elasticity. This physical condition is dependent upon the quality of the blood, and modifications of it are

probably invariably of toxic (organic or inorganic) and most frequently, infectious, origin.

The musculature of the blood vessels is automatic in exactly the same way, though not in the same degree as is the cardiac muscle. Also it is affected in a similar way by the vasomotor system, which corresponds to the vagosympathetic system of the heart.

So long as the quality of the blood is normal, the con-

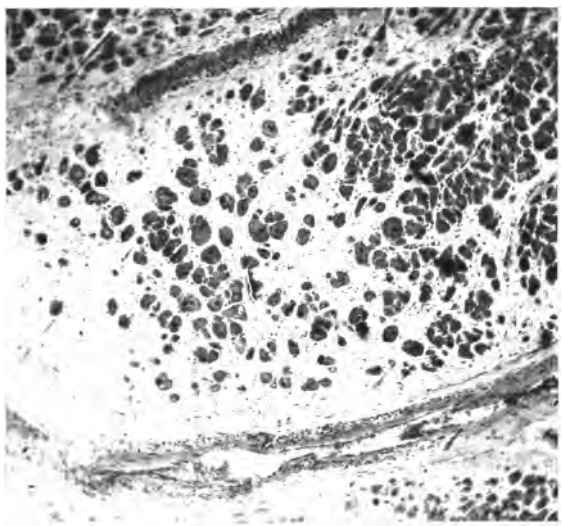


Fig. 40.—Myocardial fibrosis. The figure shows the presence of increased amount of fibrous tissue between the muscle fibers of the heart. When it is realized that practically all of the area included in the photograph should be composed of muscle it will be seen to what an extreme degree the efficiency of the heart is decreased by loss of functional tissue. When so much of the muscle is lost the rest of the myocardium must do additional work to make up for the loss (hypertrophy), and when this remainder becomes overworked the heart fails, is less able to contract, and the cavities are dilated.

dition of the musculature remains normal, and the blood pressure is preserved at a normal level. But let the quality of the blood vary and immediately the condition of the muscles is modified so that either it responds to otherwise inefficient stimuli, and contracts, or fails to respond even to normal stimulation and relaxes. In the first case the blood pressure rises and increased work is

thrown upon the heart. In the second case the blood pressure falls, and again increased work is thrown upon the heart, or, the extreme may happen, all incentive to work is removed from the heart and it ceases.

A consistently high pressure produces one or two effects. It leads to cardiac hypertrophy and it leads, if it persists, in hypertrophy of the muscular coats of the arteries (so long as the supply of food is sufficient), or to degeneration and atrophy of the muscular coats (if the food supply is not equal to the demands).

In toxic conditions the same things are true but are

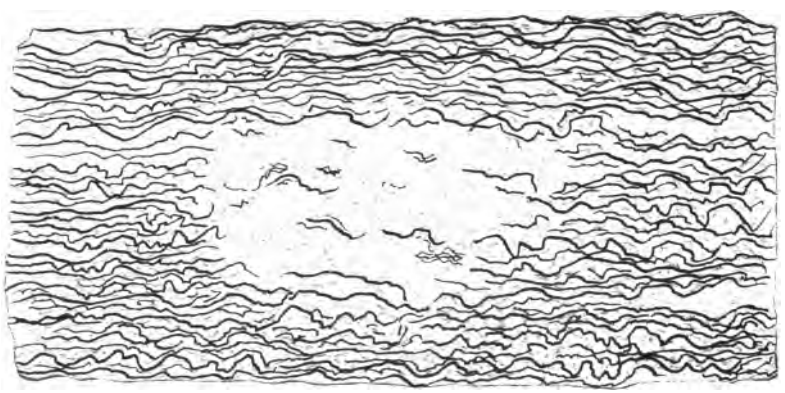


Fig. 41. Atrophy of elastic tissue in wall of the aorta in atheroma. The elastic tissue is replaced by dense fibrous tissue. (Delafield and Prudden.)

merely modified by the abnormal conditions which bring it about that fatigue of the muscles occurs earlier, and the gross lesions are more apt to be focal, particularly in those of infectious origin.

When the muscle of the vascular system is damaged so that strain of the walls occurs, the stimulus of the strain is felt by the fibrous elements. The results of this in the vessels is the same as in other tissues, namely, fibrous hyperplasia, and since fibrous tissue is not elastic in the sense that either muscle tissue or elastic tissue is, the vessels become permanently inelastic.

Even, however, with a comparatively high grade of inelasticity, the circulation may be maintained at a level consistent with the nutrition of the tissue. But let the lumens of vessels be diminished in caliber and the nutrition of the tissue suffers. Diminution of caliber occurs when there is a diffused toxic substance present in the blood; for instance, in lead poisoning. In this and similar conditions the vascular effect tends to be generalized in the smaller vessels.

In the great vessels the lesions tend rather to be focal than general, for the reason that the toxic effects tend to be produced first in the neighborhood of the vasa vasorum, in and about which the lesions are similar to those which occur in the smaller vessels, especially the arterioles, elsewhere.

In old individuals, and in the absence of infection arteriosclerosis tends to appear as a combination of degenerative process, which involves the muscularis, associated with fibrosis. In such cases the lesion is a senile one. But the more serious form is that which occurs in younger persons and which is associated with, and characterized by, the changes we call inflammatory. This form is characterized by the very common syphilitic aortitis.

Arteriosclerosis:

Infections—(aortitis, arteritis).

Noninfectious—senile arteriosclerosis.

It is in arterial conditions that are characterized by focal degeneration and inflammation that abnormalities of the normal form of the lumen, such as dilatations, tend to appear. Such dilatations are called aneurysms. Such abnormalities occur also as a result of trauma, which produce localized weakening or breaks of continuity of the vessel walls. When the vessel wall forms the wall of an aneurysm, we speak of a true aneurysm. When it does not, we speak of a false aneurysm.

It has been claimed by many that in the production of aneurysm, strain is the most important factor. This has been said because aneurysms tend to occur in individuals who do heavy work. It seems however that strain is entirely secondary; that it is active only because preceding it the vessel wall has been damaged so that a sudden increase in blood pressure is able to overcome the resistance at a diseased part.

The blood vessels may also be affected by the inflammatory process (arteritis, phlebitis), which do not lead to sclerosis. In some instances the vascular involvement follows a perivascular disease, in others it commences intravascularly (septicemia, septico-pyemia, embolism, etc.). Such inflammatory conditions result very commonly in interruption of the blood flow.

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CHAPTER X.

THE URINARY SYSTEM.

This system is composed of the kidneys, the ureters, the urinary bladder and the urethra. In the kidneys the wastes of the body (free water, salts, and various other substances) are separated from the blood, and passed into the ureters and bladder and thence into the external world through the urethra. Lesions of the kidney result in retention of toxic materials in the blood. Lesions of the other parts of the tract cause interference with the discharge of urine.

The Nephroses.

The term nephrosis is an inclusive one. It includes all the diseases except tumors from which the kidneys suffer, from mere edema to the true inflammations, whether suppurative or non-suppurative. It therefore includes what we speak of as nephritis, or Bright's disease.

The term nephritis includes two conceptions: one of them clinical, the other histologic, or if you please anatomic. Clinically it means the presence of certain qualitative or quantitative urinary variations, which are, generally speaking, increase or decrease of the total amount of urine and the presence of albumin and casts in the urine. In the anatomic sense it means this and something more. It means inflammation, which is to say the kidney is the seat of certain vascular and perivascular changes which we associated with a very distinct histologic picture, in which vascular dilatation, congestion,

and exudation are in the foreground. Albumin and casts in the urine may be produced by any process which disturbs sufficiently the nutrition (or metabolism) of the renal cells. Inflammation is one such process.

There are three main types of renal lesions. The simple nephroses, including simple edema and simple necrosis; the nephritides or inflammatory nephroses; and the renal atrophies, including the arteriosclerotic and diffuse nephroses.

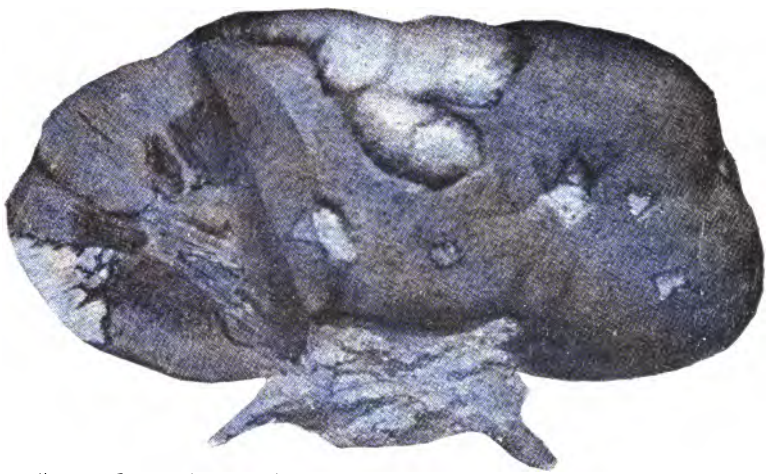

Fig. 42.—In the kidney depicted in the illustration there are several infarcts of the white variety. These lesions if they are infected may undergo suppuration. If on the other hand they are "bland" they tend to heal by granulation and organization.

The Simple Nephroses.

This group is one which is fundamentally the most important. In it are included all those types of renal disturbance which are the result of partial or complete lack of oxygen, from the edema of the athlete, and that of the soldier on the march, both of which are benign and transient, to the sudden complete necrosis of infarction. In it belong the toxic necrotic conditions which are the result of the action of organic or inorganic poisons. In all these albumin and casts appear in the urine; in all the quantity of urine is diminished. The main dif-

ference that needs mention in discussing these simple nephroses, is that in the kidney, of edema, the organ may return to a completely normal condition very rapidly; in the toxic degenerated and in the infarcted kidney, the chances are that this does not occur, but that an increase of scar tissue is found as a part of a secondary inflammatory process. In the case of the infarcts, the scarring is localized; in cases of certain chemical intoxications, it is diffuse.

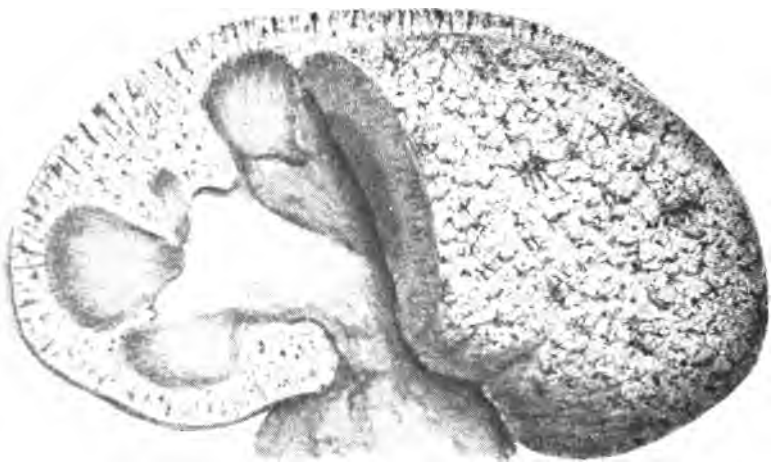

Fig. 43. An example of "chronic parenchymatous nephritis." Note that it is larger than normal and that it is exceedingly pale.

The Atrophies.

Similar in some respects to the simple nephroses are the atrophies. These, like the former, depend for their urinary phenomena upon lack of oxygen, but the cause in this instance lies not in the composition of the blood, but in the condition of the blood vessels, which have been so changed by one or another factor, that the blood, qualitatively perfect though it be, does not reach the cells in sufficient amounts over long periods of time to keep them at a physiologically active level. What happens to the

kidney in arteriosclerosis is exactly what would happen to the kidney of a modern simple edema, provided the edema were chronic, which is to say, provided the circulatory conditions remained the same. In the renal edema of the sprinter, the oxygen supply in the blood is not quite sufficient for the cells of the kidney. In the arteriosclerotic kidney, the oxygen in the blood is sufficient but it cannot reach the cells rapidly enough. The

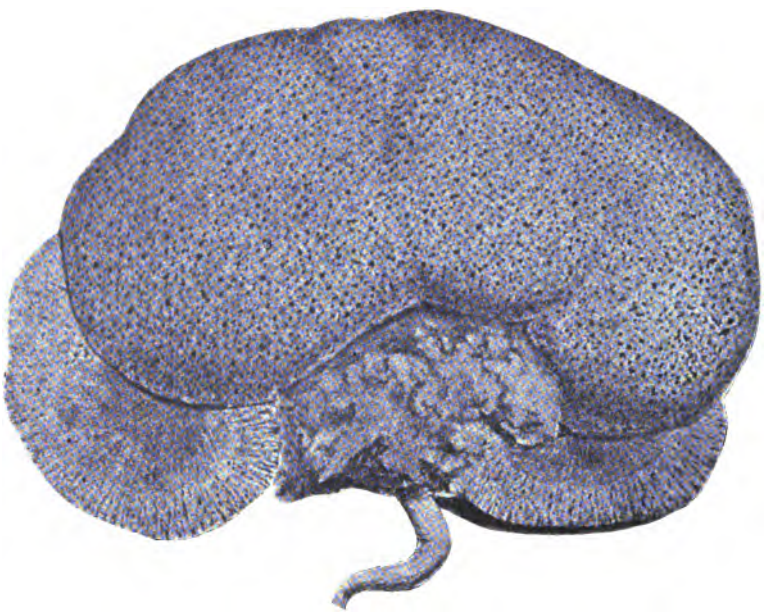

Fig. 44.—A specimen of acute nephritis associated with multiple fine hemorrhages. Note how diffusely the kidney is affected. It is also evidently swollen. Such an organ will obviously lead to a decreased output of urine.

result of this decreased access of the cells to oxygen is that they undergo atrophy, become smaller, and some of them disappear, or if the progress of the vascular disease is somewhat more rapid they undergo degeneration and disappear, and in vanishing leave the stroma of the organ apparently more abundant, relatively increased, and this tends to produce the appearance of sclerosis or fibrosis in the organ. Actually such an atrophic organ

contains no more fibrous tissue than a normal organ,—it merely possesses less parenchyma.

The Nephritides.

This group of the nephroses is characterized, so far as the renal parenchyma is concerned, by all the anatomic changes which are present in the former groups, and by certain other features, which are clearly inflam-

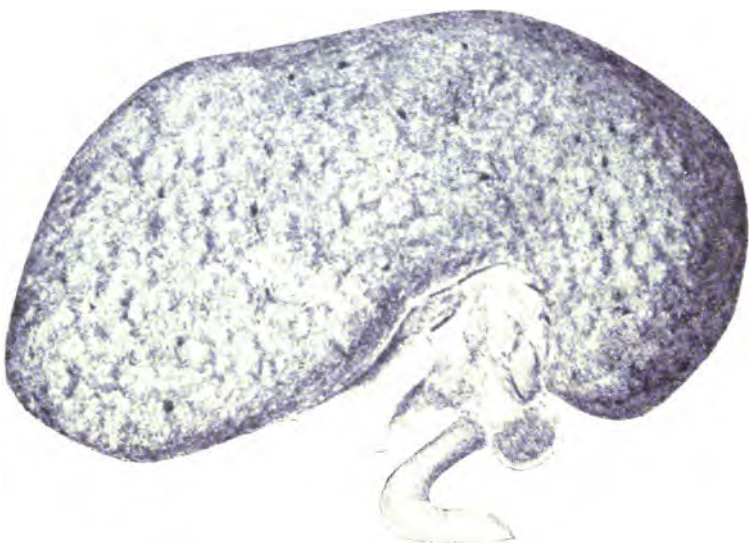

Fig. 45. As time goes on with a chronic diffuse nephritis, there is a gradual decrease in the amount of parenchyma and an increase in fibrous tissue. The organ becomes smaller and more or less distorted in shape. Such an organ is referred to as one of "secondary contraction."

matory. In all the types one phenomenon dominates the picture, and that is the one we term exudation which may or may not be associated with fibrosis. It is from the obviousness of the associated fibrosis that we are led to speak of an acute or a chronic inflammation. Fibrosis in the absence of exudation does not spell inflammation, though it may be a sequel of it. A sclerotic kidney is not necessarily one of interstitial nephritis.

It has been customary to speak of parenchymatous and

interstitial nephritis, and of hemorrhagic and suppurative, and as glomerular, tubal, and diffuse, and further as acute and chronic. These terms are however merely helpful in characterizing nephritides from the standpoint of general extent. The process in all the cases is the same. It varies only in the extent to which it affects the kidney, in the type of exudation, and the rapid-

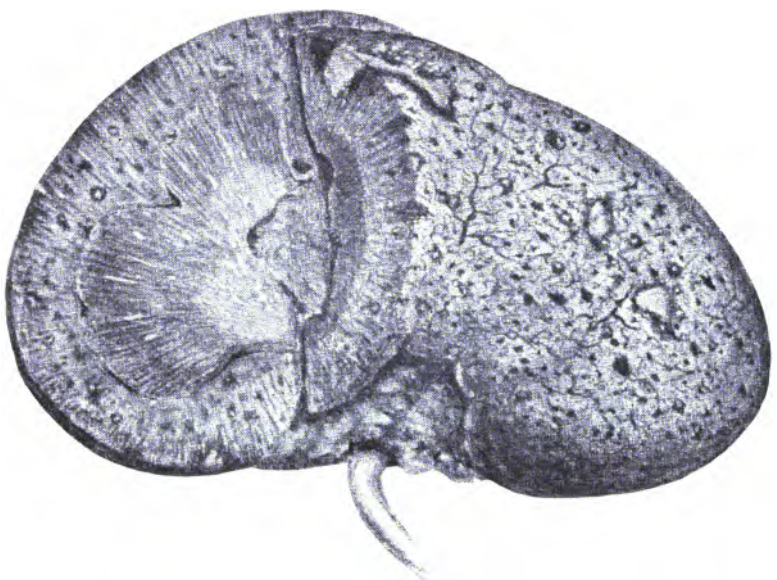

Fig. 40.—The so-called "embolic kidney." The lesions are due to the presence of small pieces of infected material which have reached the kidney from some other part of the body. Not infrequently this material comes from vegetations on the heart valves. The lesions are small abscesses.

ity of its development. All forms of inflammation are essentially interstitial in type, and the peculiar and sometimes characteristic changes which one observes in the parenchyma are secondary ones due to disturbances of metabolism resulting from poisons which reach the cells from foci of inflammation, or from lack of oxygen which is the result of perivascular conditions. There are times when these secondary changes dominate the picture; when the parenchyma has undergone fatty or soapy de-

generation, as, for example, in the "large white kidney." Under such circumstances we have been in the habit of speaking of a chronic parenchymatous nephritis, a designation which we may preserve provided we realize that it is but a type of interstitial nephritis with abundant secondary degeneration—a *diffuse nephritis*. This is very reasonable, because if we study the other classical type of kidney, the "small red" one, we find similar changes, though not so evident. In this the focal inflammatory fibrosis dominates the picture, and obscures the parenchymatous changes. In all nephritides parenchyma and interstitial tissue are both affected, but in

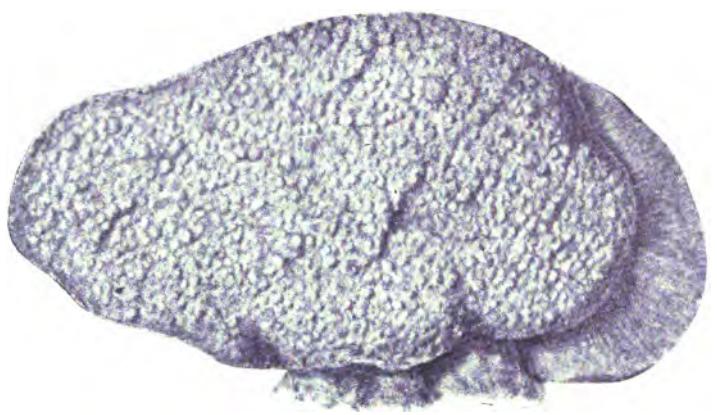

Fig. 47.—When the smaller blood vessels of the kidney are generally affected by the arteriosclerotic process, or when there is in the kidney a chronic interstitial inflammatory process going on, the kidney becomes generally contracted and finely granular as to its surface. Such an organ is called that of "chronic interstitial nephritis."

one the degenerative changes predominate; in the other, the productive. Perhaps it is best to speak of diffuse and focal nephroses. All of these remarks apply equally to the suppurative and tuberculous kidneys. In these the only difference is that the lesions tend to be more obviously and completely focal than even in the interstitial form, and therefore they acquire specific characteristics.

Now this would all be very simple were the forms of

nephroses simple, which, as a rule, they are not. As a rule they are combined, at least this is apt to be almost completely true except in cases in which death has been produced suddenly by trauma. That the conditions existing in the kidneys may undergo sudden changes is shown in many clinical cases. For instance, a person who has a well developed interstitial type of nephrosis does very well for long periods of time. The vascular and perivascular changes have advanced to such a stage

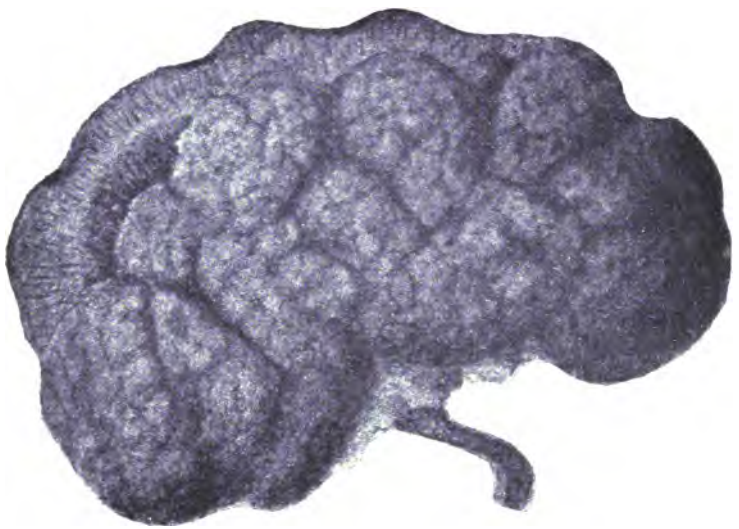

Fig. 48.—When the larger vessels of the kidney are affected by the arteriosclerotic process and when this process is not as diffuse as in the former type, the kidney becomes focally affected and contracted. It is then known as the "arteriosclerotic kidney."

that the compensatory powers of the organ are quite limited. Much of the parenchyma has disappeared, but the portion which remains is physiologically active and produces a normal amount of fluid, with little or no albumin and few or no casts. If at such a time he meets a sudden traumatic death, the kidney would appear as a "small red kidney," a primarily contracted kidney. But let him suffer an attack of enteritis; let him absorb a

few more colon bacilli; a too large quantity of poison—and he dies in uremia and the kidney at postmortem is apt to be gray and then we are apt to say that it is a "secondarily contracted kidney," or small gray kidney. And it is quite probable that under such conditions unless he makes use of the clinical details, the pathologist may insist that what he finds tells the whole story.

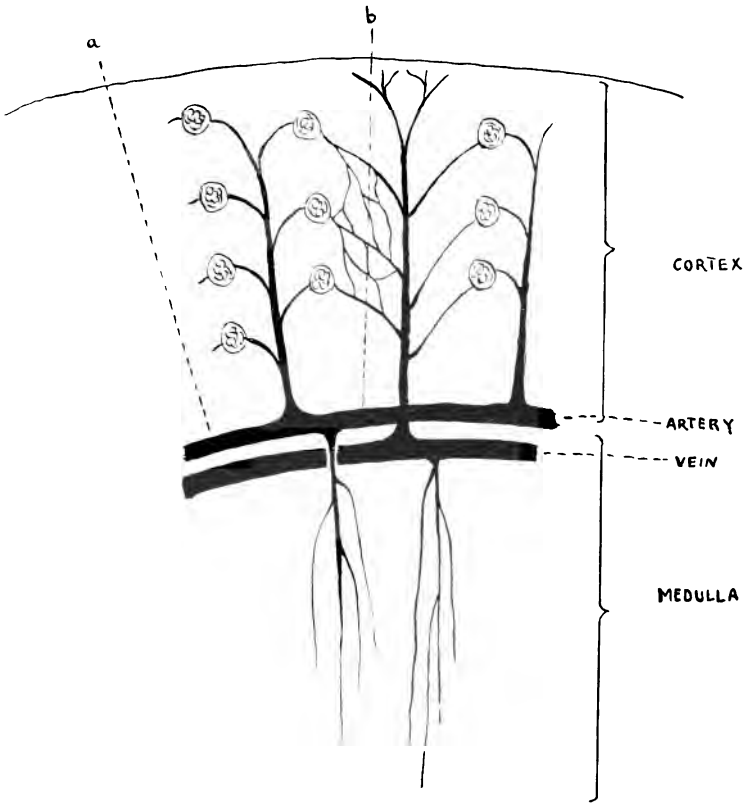

Fig. 49. This illustrates very schematically the blood supply of the kidney. It shows that the collateral blood supply between the anatomic parts of the organ is a very slender one that the arteries of the kidney like those of the spleen, lungs, intestine, heart, and brain, are functional or physiological end-arteries. From the standpoint of vascular disturbances, this means that a sudden blocking of one of the end arteries (embolism) will result in death of the tissue in the area supplied by the obstructed vessel (infarction), and that gradual closing of the vascular lumen (arteriosclerosis, or thrombosis) will lead rather to atrophy of the tissue. Atrophy of this area will lead eventually to decrease in volume while adjacent areas will retain their size, or, because of the additional work thrown upon them, will become somewhat larger (compensatory hypertrophy). The result will be a surface with a depression for each area of atrophy (granular kidney).

Classification.

It would seem then that for the sake of simplicity the following classification would be serviceable:

A. The diffuse nephroses—(acute intoxication).
   Simple edema, and necrosis.
   Acute diffuse nephritis (acute Bright's).
      Glomerular nephritis.
      Hemorrhagic nephritis.
   Chronic passive congestion.
   Chronic diffuse nehpritis (chronic parenchymatous nephritis).
      Glomerular nephritis.

B. The focal nephroses—(vascular or infective).
   Infarction.
   Arteriosclerosis.
   Acute interstitial (septic or simple) nephritis.
   Chronic interstitial nephritis.

C. Combinations of focal and diffuse forms.

Such a classification has one value, if no other, namely, that it allows of a better understanding of the urinary findings, that is to say it permits the clinician and the pathologist to stand a little closer together.

Urinary Changes in the Nephroses.

I. Diffuse nephroses—(acute and chronic).
   Decrease of urine.
   Casts present.
   Albumin in very noticeable amounts.

II. Focal nephroses—
   A. Acute—
      Urine may be decreased depending upon the number and extent of the lesions.
      Casts present.
      Albumin in moderate amounts.

B. Chronic—

Little or no decrease of urine.

Few or no casts (these come from the diseased foci).

Little or no albumin.

III. Combination forms—

The urinary changes vary.

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CHAPTER XI.

THE RESPIRATORY SYSTEM.

The respiratory tract is a system of organs by means of which the oxygen of the air is taken into the body and so distributed that it can be absorbed into the blood. It also acts as the means by which the body is able to rid itself of a certain proportion of the gases formed within the body and held in the blood. This interchange of gases takes place in the alveoli of the lungs from which there is a clear passageway to the exterior of the body. Any lesion which disturbs this interchange is important because it interferes with the ventilation of the body.

External respiration may be disturbed by limiting the amount of air which can be inspired, or by limiting the ability to inspire. In the first case we must consider the quantity of air surrounding the body. In the second case we have to deal with effects which prevent expansion or contraction of the normal lungs or with changes in elasticity in abnormal lungs. On the one hand the lungs are unable to expand because of extrinsic difficulties; on the other, because of intrinsic ones.

Extrinsic conditions—(exclusive of qualitative or quantitative variations in the surrounding air).

Any extrapulmonary pressure.
Fluid in the pleural cavities.
Air in the pleural cavities.
Pleural adhesions.
Paralyses of the respiratory muscles.

Intrinsic conditions—

Acute inflammations.

Pulmonary fibrosis (chronic inflammations; konioses).
Edema.
Emphysema.
Bronchial inflammations.
Muscular contraction of bronchial muscle (asthma).
Tumors.

Internal respiration (gaseous interchange) is modified by variations in the quantity and quality of the blood which passes through the pulmonary and bronchial vessels and by variations in the area of the respiratory surface. The rate of the blood flow is an important factor in internal respiration, since when the blood flow is slow, as in chronic congestions, carbon dioxide tends to accumulate in the blood just as surely as though respirations were partially suspended. When such a condition arises a secondary condition of edema tends to be produced which has a direct effect upon external respiration. On the other hand, when the respiratory surface is diminished as is the case in the pulmonary consolidations, the air has not the normal access to the walls of the alveoli where the gaseous interchange takes place.

Blood and vascular conditions—
Slowing of the pulmonary circulation.
Chronic passive congestion.
Arteriosclerosis.
Interference with the bronchial circulation.
Edema.

Pulmonic conditions—
Consolidations.
Bronchial obstruction.

The most frequent abnormal pulmonary conditions are infectious in origin and although they are preeminently toxic in their effects on the body as a whole, they also produce mechanical difficulties which result from the ef-

fects upon respiratory surfaces, that is to say, from the edemas and the frequently associated inflammatory changes.

The mechanical effects follow several sorts of causes, chief among which are the obstructions, complete and incomplete. Among the latter are the stenoses. The chemical effects are illustrated in the infections, particularly in cases in which less than half the pulmonary tissue is involved, or in other cases, like diphtheria, in which there

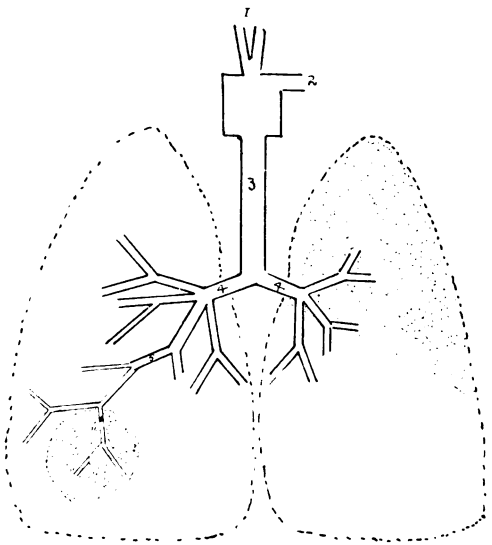

Fig. 50. This illustrates schematically the respiratory tract with the two nares (1); the mouth (2); the pharynx and larynx, the trachea (3); the main bronchi (4), and the terminal bronchi. If the nares are obstructed, respiration is carried on through the mouth. In the upper respiratory tract there are therefore alternative pathways for the air. If, however, the trachea is obstructed, the entrance of air tends to be completely cut off. At the epiglottis an edema of comparatively slight degree may produce asphyxiation. The farther one proceeds out in the respiratory tract, the less danger is there of asphyxiation. The small rounded area illustrates what is meant by a focus of lobular pneumonia (bronchopneumonia). The larger area is intended to represent an area of lobar pneumonia.

may be no hindrance to inspiration or expiration. Since it has been shown that a gradual reduction of the pulmonary tissue to one-sixth the normal amount is compatible with life, it will be apparent that the majority of pulmonary lesions are important rather from the chemical than the mechanical point of view, and that

except for a relatively small group of cases, most of the lesions of the respiratory tract are of vital importance because of the chemical conditions that develop.

If we consider the anatomic arrangement of the respiratory tract we find that it is composed of three anatomically (mechanically) important parts—the nasal part, the tracheal part, and the bronchial part.

The *nasal portion* forms the normal entrance for air. It serves as a warming oven, and as a filter. It is only when it is damaged in one or another way that the accessory path (the oral) is used. When this accessory path is used the air is not sufficiently warmed or filtered, and the opportunities for irritation and infection of the pharynx, trachea, bronchi and the lungs themselves are multiplied. One of the most frequent causes of disease of the nasal passages is adenoid growths in the pharynx; another is inflammation of the mucous membrane of the nasal cavities with consequent swelling of the tissue (coryza).

The *tracheal portion* of the tract is a single pathway. It therefore is that part of the respiratory system in which a mechanical defect produces the most serious results. External pressure of enlarged adjacent organs, such as the thymus or lymph glands, often produces the most serious effects, as illustrated in edema of the glottis and inflammations, often producing effects upon the respiration altogether out of proportion to the size and extent of the lesion.

The *bronchial portion* of the tract begins as a double pathway, which rapidly breaks up into many fine subdivisions, the bronchioles, which terminate in the infundibula and air vesicles. In this part of the tract there are many opportunities for damage which may produce little or no general disturbance. This is especially true of the mechanical effects. It makes a great deal of difference, however, whether an obstruction occurs in one

of the main bronchi or in one of the small bronchi because the nearer to the trachea an obstruction exists the greater the area of respiratory surface which is affected.

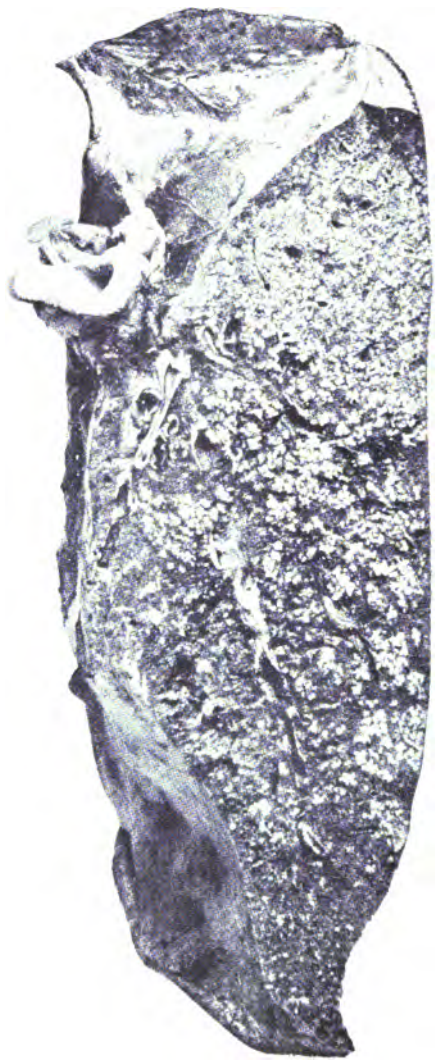

Fig. 51.—Lung. Subacute tuberculosis with some fibrous overgrowth towards upper part of lung, and showing acute peribronchial spread into the lower lobe. (Edinburgh University Anatomical Museum. Catalogue No. R.C.e.6.) (Beattie and Dickson.)

The rapidity with which an obstruction develops is a very important item in the production of symptoms, for whereas five-sixths of the lung tissue may be eliminated

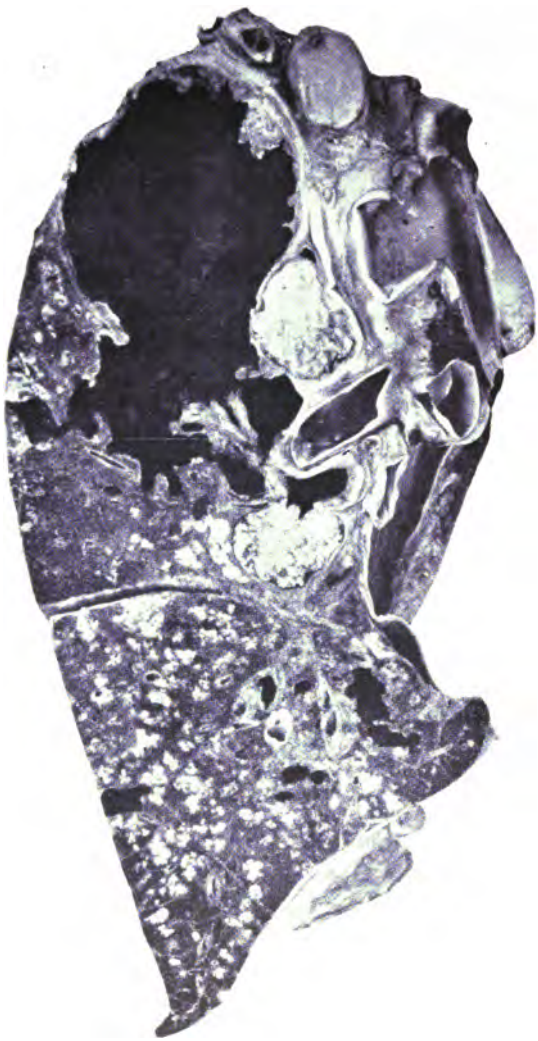

Fig. 52. Lung. Chronic phthisis, showing a large irregular cavity in the upper lobe. In the lower lobe there are scattered acute nodules grouped in clusters around the small bronchi; and also several small more acute cavities. The bronchial glands are enlarged and caseous. (Edinburgh University Anatomical Museum. Catalogue No. R.C.g.10.) (Beattie and Dickson.)

if this be done only gradually, a sudden obstruction which involves less than one-half of this same tissue may and not infrequently does prove fatal. In certain cases of pulmonary tuberculosis one finds that at least three-fourths of the respiratory surface has become valueless, functionally, before death has occurred, but a perforation of the pleura which allows air to enter the pleural cavity (pneumothorax) and compress one lung, may prove fatal.

The causes of respiratory insufficiency are as follows:

I. Physical—(disturbances of ventilation).

Obstructions to entrance and exit of air:

Nasal—Hyperemia, including the inflammatory type, septal deformities, turbinate deformities, foreign bodies, tumors.

Pharynx—Adenoid growths, edemas, peritonsillar and peripharyngeal inflammations, tumors.

Larynx—Edema of the glottis, acute inflammations, tumors, paralyses.

Trachea—Inflammations, external pressure (thymus, thyroid, lymph glands), foreign bodies, paralyses.

Bronchi—Inflammations, muscular spasm (usually associated with edema), foreign bodies, pressure of enlarged lymph glands (tumors, inflammation).

Lungs—Edema, chronic congestion, infarction (embolism), inflammations, tumors.

Loss of elasticity including increased external pressure (limitation of expansion).

Pulmonary fibrosis (anthracosis, chronic passive congestion).

Emphysema, pneumothorax, hydrothorax.

The chemical factors in pulmonary disease are, as a rule, associated with abnormal physical conditions.

II. Toxic—(disturbances of metabolism).

Bacterial—The inflammations, pneumonias, bronchitides, laryngitides, tracheitides.

Irritating gases—Ammonia, chlorine, sulphurous acid, etc.

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CHAPTER XII.

GASTROINTESTINAL SYSTEM.

What we call gastrointestinal diseases are expressions of alterations of function in one or more parts of the gastrointestinal system. They are commonly confused with symptoms, such as hyperacidity, hypoacidity, hypermotility and hypomotility, which are not diseases, but symptoms of disease. Sometimes they are associated with symptoms in other parts of the body than the gastrointestinal tract, and such symptoms call attention to the fact that the various organs of the body are not truly separated or independent, but that they are actually dependent upon one another. So with gastrointestinal upsets the nervous system may be affected, or the urinary system, and it is from these distance effects that we have come to make so much of a group of symptoms, which may be combined into different complexes, in different individuals, which we call, comprehensively, gastrointestinal intoxications or, also, autointoxication.

In order to be clear in our conceptions we should consider first of all the functions of the organs comprising this tract or system.

The function of the stomach and of the intestines also is to contain and retain food for a certain period of time during which the food is chemically changed by means of ferments. In order to fulfill this function it must be capable of expansion, and, in order to expel the contents at the proper time it must be capable of returning to its original size. In other words, it must be elastic and contractile, and the elasticity and contractility are chiefly the result of the condition of the musculature. The func-

tion of the intestine is to carry the food from the stomach to the external world and at the same time to allow time for absorption of foodstuffs into the body. This function depends upon elasticity and contractility and here again the contractility is mainly dependent upon the condition of the musculature. In other words, the function of the gastrointestinal tract, so far as motility (contractility) is concerned, is dependent upon the condition of the muscularis, and so *disease tends to be produced by variation in the elasticity and motility of the various portions of the gastrointestinal tract.*

It is these qualities of elasticity and contractility which present stasis in the intestinal tract. Normally the various segments of the tract act in such harmony that the contents are gradually pushed along to their normal destination in a certain normal time. A healthy bowel will not permit of stasis but will carry on its motor functions with ease and regularity. To assist in this function there must be a coordinating or regulating mechanism. This Keith believes he has found in the myenteric (Auerbach's) plexus. He finds that at certain points this plexus is concentrated to form masses (or nodes) which correspond to the nodes in the conducting tissue of the heart, and that at these nodes new rates of peristalsis are inaugurated and persist throughout the segment to which they belong. Evidently *disease of the gastrointestinal tract may occur because of interference with, or damage to, the myenteric coordinating system.*

In order that the food shall be properly prepared for absorption, the necessary kinds and amounts of ferments must be secreted by the glands of the gastrointestinal tract and by the accessory glands, and in order that these shall act properly the contents of the tract must have the proper chemical reaction. In the stomach the reaction must be acid; in the intestine it must be alkaline.

Therefore *variations in the quantitative secretion of the various digestive fluids and in the qualitative composition of them, tends to produce disease.*

Gastrointestinal disease arises from abnormal changes in elasticity, motility (contractility), segmental coordination, secretion of ferments, and (chiefly) chemical reaction.

When we consider these four groups we find that we can most usefully combine them into two large groups, for we find that changes in elasticity and motility are apt to occur together; and that changes in production of ferments and the chemical reaction of the juices are apt to be combined. Also we discover that each of these groups are interwoven to such an extent that it is not possible to separate them completely.

The normal course of events in gastric digestion is briefly as follows:

Food enters the stomach and is there kneaded and thoroughly mixed with gastric juice so that the ferments, chiefly pepsin, may act upon the proteins. For the ferment action, a certain degree of acidity is necessary. After a certain time the partially digested food is expelled through the pylorus and enters the duodenum.

What we call gastric indigestion may depend upon a break at any point in this process, i. e., the muscular movements of the stomach may not be sufficiently active to produce thorough mixture of the food and the gastric juice; the gastric juice may not contain sufficient pepsin to accomplish a normal result; the acid content of the gastric juice may be below or above normal, and then in either case the food may be held too long in the stomach and then undergo abnormal changes which lead to more or less disturbing symptoms or distress.

How shall we account for variations in gastric motility? There is a variation that occurs normally and which depends upon the nature of the ingested food.

For instance, carbohydrate foods pass through the stomach most rapidly, proteins are next and fats are slowest. We can say at once then, that a diet very rich in fats will hinder the passage of foods through the stomach. Moreover the ingestion of oils decreases the amount of gastric juice, while ingestion of proteins increases it, and carbohydrates (bread) produce a juice of greatest digestive power. These facts account for the ordinary effects of dietary indiscretions which are commonly transient, but which may persist, if the indiscretions are persisted in, and produce other less transient effects resulting in structural changes.

Now it is quite possible that these normal variations in motility are the result of modification in the acid content of the gastric juice. We know the opening and closing of the pylorus are due to the reaction of the food—i. e., they depend upon the presence of a certain amount of free acid. We know that ingestion of carbohydrates produces an abundant active secretion, and we know that carbohydrates are less active in neutralizing the acid (by chemical combination) than the proteins which also produce an abundant secretion. We would expect then, that the carbohydrates would pass through the stomach more rapidly because they permit the acid to accumulate, and that the proteins would remain longer in the stomach because in combining with the acid they reduce the acidity of the gastric contents. Fats and oils, on the other hand, reduce the quantity of juice and therefore the acid is slow in accumulating.

When the emptying of the stomach is unduly impeded, there is opportunity for fermentation to occur in the contents. We constantly swallow bacteria with our food, but commonly these organisms are rendered harmless because their activities are hindered by the hydrochloric acid. With a decrease of acid they are allowed to act upon the food, and in doing this they produce abnor-

mal acids and gases. The former act upon the mucous membrane producing inflammatory effects; the latter produce distention or "bloating."

Immediately inflammation is produced, an increased amount of mucus is produced, and mucus, being alkaline in reaction, neutralizes more hydrochloric acid, and therefore assists in hindering the passage of food into the intestine. The same stimulation which produces the increase in mucus, irritates the functional cells, so that eventually they become fatigued and produce less secre-

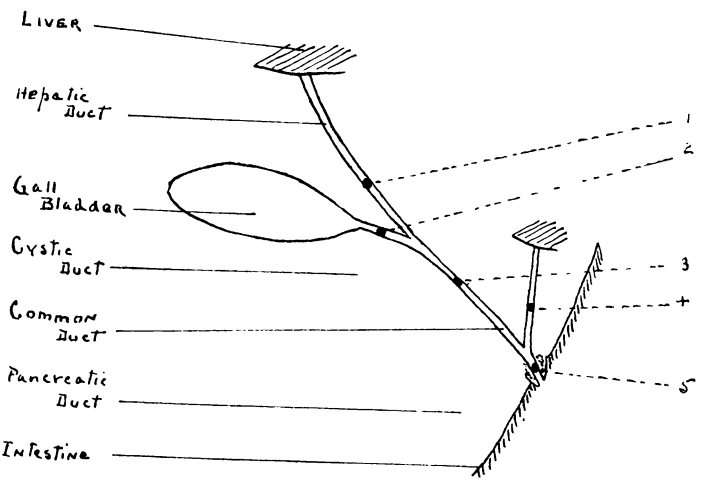


Fig. 53. This is a schematic sketch to illustrate the arrangement of the bile passages and the effects of lesions in them. Bile formed in the liver is stored in the gall bladder from which as occasion demands, it passes into the small intestine. An obstruction in the cystic duct does two things; it prevents the storage of bile, and it prevents what bile happens to be in the bladder from reaching the intestine. No clinical symptoms follow either of these eventualities. On the other hand an obstruction in either the hepatic duct or in the common duct prevents the bile from reaching the intestine and jaundice (icterus) results. Blocking of the pancreatic duct hinders the pancreatic secretion from the intestine and so leads to a certain type of indigestion. If an obstruction occurs in the common duct below the entrance of the pancreatic duct, bile may be forced into the latter and cause pancreatic disease.

tion. The result of this is that further fermentations are assisted and so (the disease we call it) becomes chronic. When this stage is reached—when inflammation has become chronic, fibrous tissue is produced in the wall of the stomach, the functional cells atrophy and disappear, the mucous membrane becomes thin and grad-

ually becomes less and less able to produce the necessary amount of acid or ferments. When this stage is reached, an incurable condition has been produced. Before it is reached, there is no incurable stage,—only each more advanced stage is less easily remedied.

But oftentimes it is not so much the relative amounts of carbohydrates, proteins, or fats that is the original cause of indigestion. More frequently it is the quality of the food or other substances that gain entrance to the stomach. Very hot food or drink, very cold drinks, alcoholic beverages, highly spiced foods—all are far more frequent causes. These act by the virtue of their irritative action on the mucous membrane. They produce hypersecretion of mucus and the related stages of fermentation that have already been mentioned, or they cause hypersecretion of gastric juice with subsequent atrophy or hypertrophy of the mucous membrane, resulting on the one hand in absence of secretion or, on the other, in more or less permanent hypersecretion.

What has been said concerning the stomach applies with very few variations to the intestines. Changes in motility, in secretion and absorption depend largely upon factors which are introduced from without, and very commonly are associated with gastric disturbances. Gastric fermentations are prone to lead to intestinal disease, and variations in gastric acidity lead to modifications in the production of pancreatic ferments. In the course of these general modifications which result from gastrointestinal disease then are produced the most various diseased conditions in other organs which cause the symptoms which belong to what we often call the gastrointestinal intoxications.

But all gastrointestinal disease does not depend upon abnormal processes which are primary in the stomach and intestines. Some are the results of changes which are primary in the liver or in the pancreas. As a result

of certain changes, quantitative or qualitative variations in the secretions of these organs are produced, and these variations are of far reaching importance.

It will be remembered that all the above-mentioned juices are poured into the intestine, immediately after the entrance of the acid gastric chyme into the duodenum, apparently as a result of the action of the acid. All the intestinal secretions are alkaline. They there-

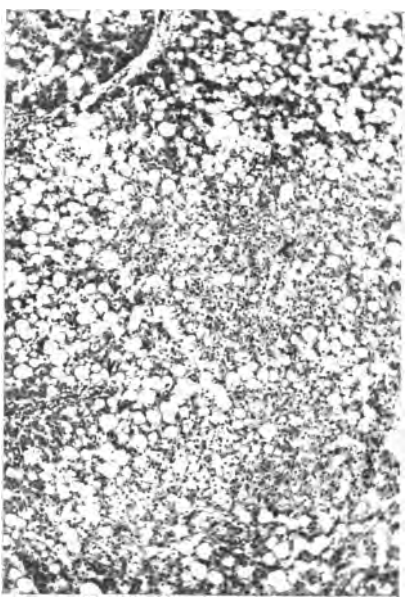


Fig. 54.—Section of a bit of "fatty liver." Note that there is fully as much fat, which appears as clear space in the photograph, as active liver tissue. Such changes occur either because the organ is not able to burn the fat brought to it or because too much fat reaches it by way of the blood stream.

fore tend to neutralize the acid of the gastric juice and therefore they produce the conditions which are necessary for opening of the pylorus. So long as the duodenal contents are acid, the pylorus remains closed. *An insufficient amount of alkaline juice from the digestive glands tends to produce disease.*

The activity of the pancreatic juice depends upon the

activation of its proteolytic pro-enzymes by enterokinase which exists in the succus entericus, which is caused to flow by the presence of pancreatic juice in the intestines. *Absence of enterokinase tends to produce disease.*

The flow of all the intestinal juices, pancreatin, bile and succus entericus, is brought about by the action of the secretion (produced in the cells of the intestines by the action of the acid gastric chyme) upon the cells of the pancreas, liver, and intestinal glands. *Absence of sufficient acid in the gastric juice tends to produce lack of intestinal secretion, and hence to produce intestinal disease.*

If the pancreatic juice is not activated, proteolytic

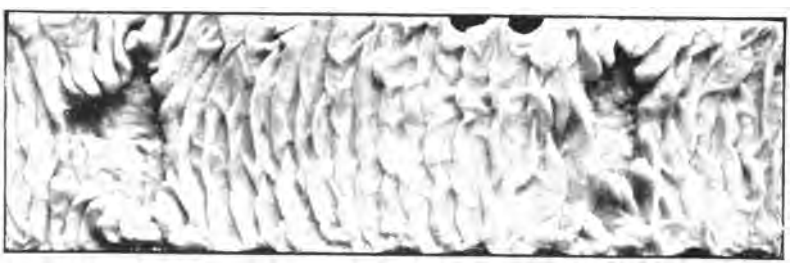


Fig. 55. Tuberculous ulcers of the small intestine. Showing the extension of the ulcers in a direction transverse to the axis of the gut. (Delafield and Prudden.)

digestion suffers. If the bile is not present in sufficient amounts, the utilization of the fats of the food is reduced or hindered. The conditions produced in this way are ones that result from insufficient preparation and absorption of food. The insufficient preparation allows of increased bacterial activity and tends to the production of abnormal substances, or substances in abnormal amounts, which, being absorbed, may give rise to intoxications, providing they are not neutralized.

But aside from these there are changes which occur in the glandular organs themselves which produce similar effects. Diseases of the liver, of the pancreas, of the wall of the intestines, produce the same effects. In

this group we have the fibroses of the liver and the bile passages which decrease the flow of bile and produce qualitative changes in it. Inflammation of the pancreas or its ducts produces quantitative and qualitative effects upon the pancreatic juice and similar changes in the wall of the intestines tend to reduce the formation of enterokinase and secretin.

Just as gastrointestinal disease may have its starting point outside that tract, in the accessory glands in the abdominal cavity, so also it may have its origin in the mouth. The mouth is the most important portal of in-

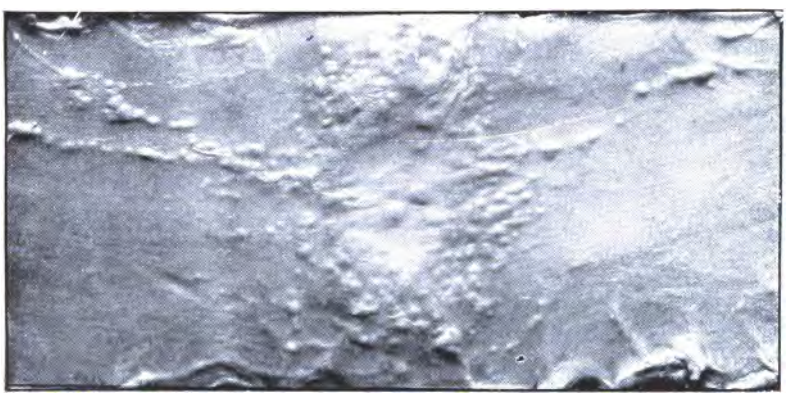


Fig. 56.—Subserous tubercles following the lymph-vessels at the bottom of a tuberculous ulcer of the small intestine. (Delafield and Prudden.)

fection of the body, and is perhaps more prone, especially in the years after the first decennium, to infection than any other part of the body. Moreover diseases of the mouth, especially those in which the teeth are involved, are every day assuming greater importance in medicine. It is becoming more and more evident that the lesions of many accepted clinical complexes are secondary to primary infections of the oral cavity and also that many obscure symptoms are the sequels of chronic focal infections which in very many cases are located in the teeth or in their surrounding tissues. Hence it

is that pyorrhea alveolaris and peridental and dental abscesses are becoming of as great importance to the physician as to the dentist, and that there is every reason to believe that, in certain directions at least, the

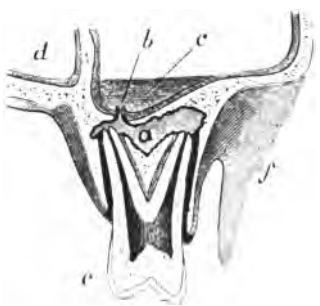


Fig. 57.

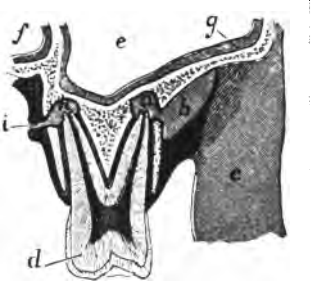


Fig. 58.

Fig. 57. - An alveolar abscess at the root of an upper molar discharging into the maxillary sinus. *a*, Abscess cavity; *b*, Mouth of sinus in the floor of the antrum; *c*, Pus in the antrum; *d*, Nasal cavity; *e*, Tooth; *f*, Tissues of the cheek. (After Black.)

Fig. 58.—An acute alveolar abscess from the buccal roots and a chronic one from the lingual root of an upper molar. *a*, Cavity of acute abscess in the bone; *b*, Pus cavity between bone and periosteum; *c*, Tissue of cheek; *d*, Tooth; *e*, Maxillary sinus; *f*, Nasal cavity; *g*, Malar process; *h*, Chronic abscess discharging at *i*. (After Black.)

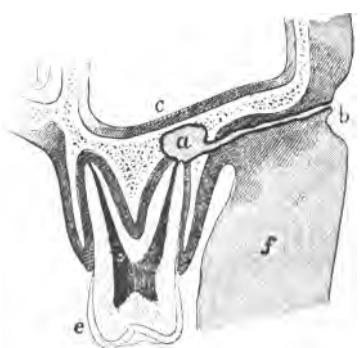


Fig. 59.

Fig. 60.

Fig. 59. -Alveolar abscess from buccal roots of an upper molar discharging on the face. *a*, Abscess cavity in bone; *b*, Sinus opening on the face; *c*, Maxillary sinus; *d*, Nasal cavity; *e*, Tooth, *f*, Tissues of the face. (After Black.)

Fig. 60.—Scar remaining from a sinus following an alveolar abscess. (After Black.)

practice of dentistry will have to be revolutionized even as medical views concerning the importance of the mouth as a source of generalized disease are being changed. It is coming to be realized that foci of infection in or about the mouth may be the starting points of such so-called diseases as rheumatism, endocarditis, appendicitis, gall-bladder disease, gastric ulcer, osteomyelitis, hay fever, asthma, urticaria, and even certain goiters. When we say in or about the mouth we have reference to the tonsils, the nasal sinuses and antra, as well as the teeth and peridental tissues.

The reason why the mouth is so apt to be a primary source of trouble is that it, more than almost any other part of the body, is exposed to the action of external injuries, and that modern habits of eating and drinking produce conditions which, without proper precautions, lay the foundations for various sorts of local and general trouble. Too hot or too cold foods taken into the mouth do two things—they injure the epithelial surfaces and so predispose to infection, and they tend to damage the teeth and make them more easily attacked by bacteria. Food which is too carefully chosen for tenderness and easy mastication, or which is finely divided, tends to collect between the teeth or along the margins of the gums, and there ferment. Thereupon inflammations or caries, or both, result. The more antique habit of not eating hash but of exercising the teeth and gums on the food made the toothbrush less essential for health than it now is. Cattle which are fed on soft food,—as, for instance, still slops,—almost exclusively, have dental trouble that animals under normal circumstances never have. It is exercise which keeps the teeth and gums in good condition and if this cannot be accomplished by means of the food, some other agent is required and this is usually the toothbrush assisted too frequently by the dentist's drill. Dental floss

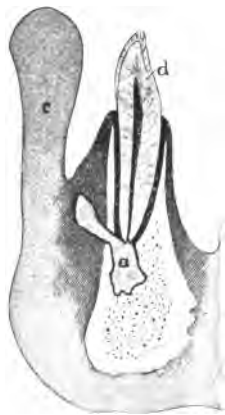
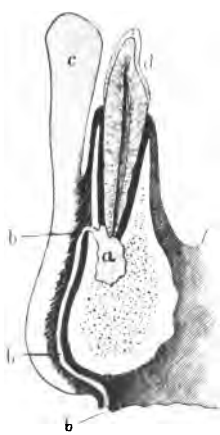


Fig. 61. Fig. 62.

Fig. 61. Acute alveolar abscess from a lower incisor "pointing" on the gum. (After Black.)

Fig. 62. Acute alveolar abscess from a lower incisor forming a pocket beneath the periosteum. (After Black.)



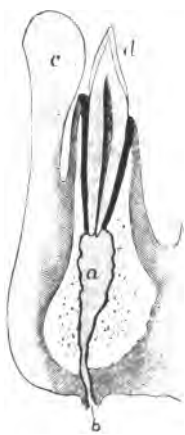


Fig. 63. Fig. 64. Fig. 65.

Fig. 63. Chronic alveolar abscess at the root of a lower incisor with a sinus opening on the gum.

Fig. 64. Chronic abscess with sinus opening through the skin beneath the chin.

Fig. 65. Chronic abscess which has involved the maxilla and finally penetrated it and the skin beneath the chin.

takes the place of the older meat fibers which stuck between the teeth and had to be picked out after the prandial exercises (or even sometimes during them). In this process the spaces between the teeth were cleaned.

From the standpoint of dentistry it is important to remember that crowns and bridge-work, as they are too commonly applied, while they may be something of a convenience, are nevertheless a very real danger in producing focal and general infections and intoxications. To the truth of this x-ray pictures of the teeth will testify. Any apparatus which tends to produce mechanical irritation is a dangerous one, for while it is true that foreign bodies may produce little or no damage provided they exist in aseptic surroundings, yet in the presence of infective organisms they act invariably to intensify the reaction between tissue and germ. A bridge which offers opportunity for the collection of food and bacteria about it; a crown or a bridge which is attached to or which covers a tooth whose nerve has been killed (by which procedure the tooth itself has been made a foreign body), especially if complete sterilization has not been carried out, is a menace to the general health of the patient, who had far better have fewer teeth than such an appliance. A little macerated pulp at the bottom of root canal and one living bacterium buried at the bottom of a root canal under an impervious cap or filling, is not to be preferred to a vacant space in the tooth line. It is under such conditions that root and alveolar abscesses develop and remain for long periods of time affecting the health of the individual by producing bacteria and toxins to enter the blood stream by which they are carried to the heart, central nervous system, muscles, bones, or other tissues and organs.

Recent studies of the teeth make it increasingly evident that to care for these instruments, especially with regard to the root canals, is extremely difficult for me-

chanical reasons if for no others. As long as it was believed that each tooth had a single pore at the tip of each root it seemed simple enough to completely remove the dead nerve and its surrounding tissue. But when, as Cassidy has shown, there may be, not merely several terminal pores, but also lateral canals and pores, then indeed is the problem accentuated, for there is little chance that an instrument can be devised to enter these lateral passages. And evidently the dead tissue should be completely removed. Dead tissue is always a source of danger, offering as it does a favorable medium for bacterial growth, and even small remnants of such nutri-

Fig. 66. A photograph from a smear preparation from material beneath an apparently perfect crown on a bicuspid tooth. In this case there was absolutely no visible defect in either tooth or crown. (Photo by Goosmann.)

ent material may lead to the production of a focus of infection which may have a tremendous influence on the body as a whole. Such things as these emphasize the necessity of perfect aseptic (and antiseptic) technic in operations upon the teeth no less than in surgical operations upon other parts of the mouth.

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CHAPTER XIII.

THE NERVOUS SYSTEM.

The nervous system is the chief mechanism in bringing about the adjustments of the organism to its environment, and therefore upon it depends in a very large measure the preservation of the species. It consists of a mechanism which receives stimuli and transmits impulses, a mechanism for adjusting reactions to stimuli,

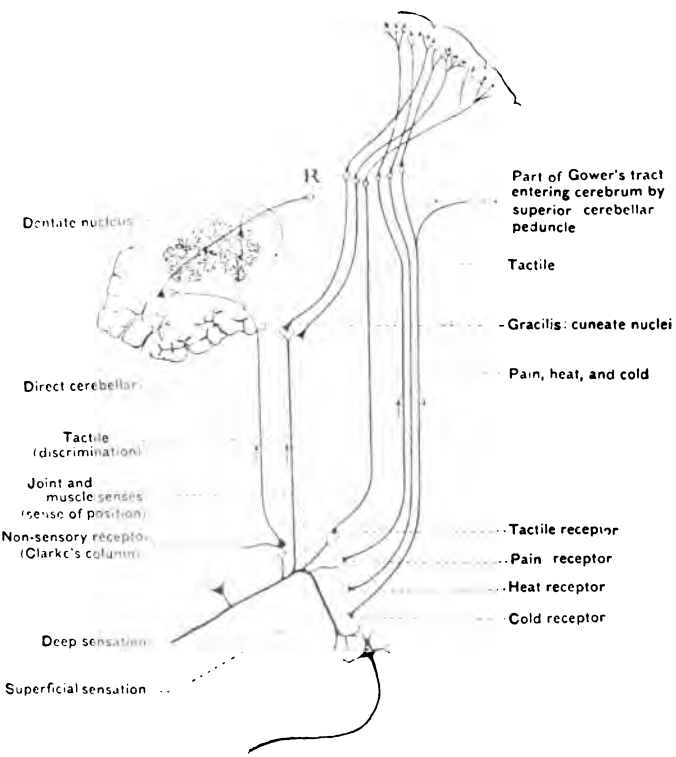

Fig. 69. - Diagram to illustrate afferent systems to cerebrum and cerebellum. (After Mott and Sewell.)

and a mechanism for preserving and correlating impressions. By means of these, stimuli are localized and responses coordinated, and, in some manner which we do not understand, associations are formed upon which are

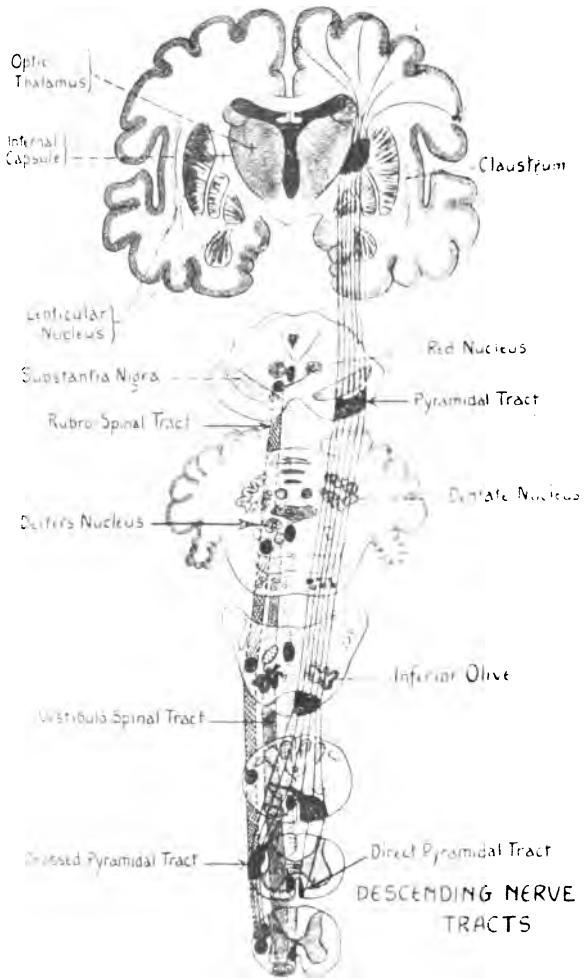

Fig. 67. Schema of course taken by chief descending tracts of brain stem. (Gordon Holmes.) The tract in red, to the right of the rubro-spinal tract, includes the posterior longitudinal bundle, together with the fibers of the thalamo-spinal and tecto-spinal tracts. (After Mott and Sewell.)

founded memory, thought, will, judgment, and the emotions.

Interference with conduction in any part of the system leads to variations in the status of the organism by

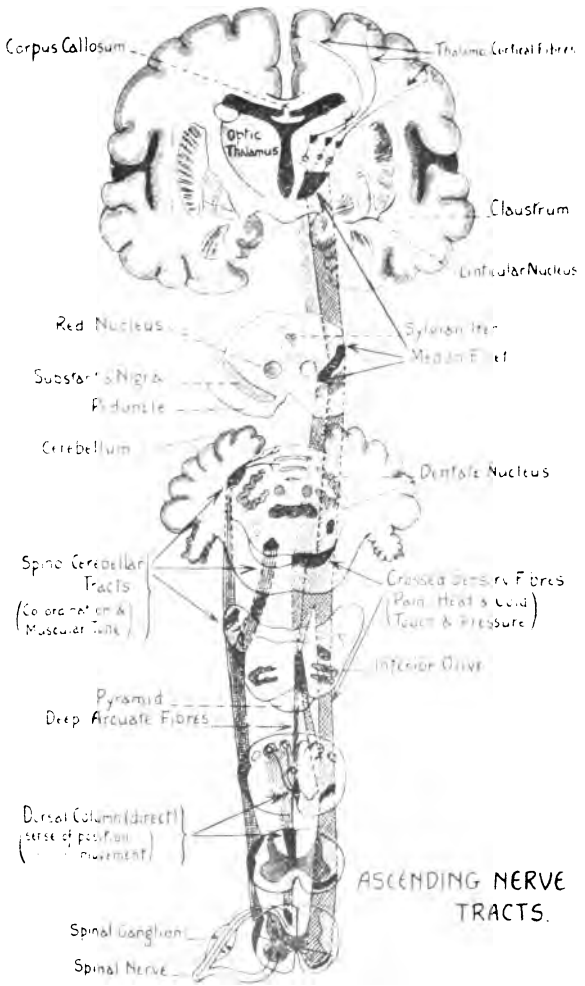

Fig. 68. Diagram of ascending tracts between the spinal cord and brain (Gordon Holmes), with the probable path of sensory impulses. (After Mott and Sewell.)

causing abnormal responses to stimuli. In some individuals conduction is slow; in others, it is rapid, but in either it may become slower or more rapid depending

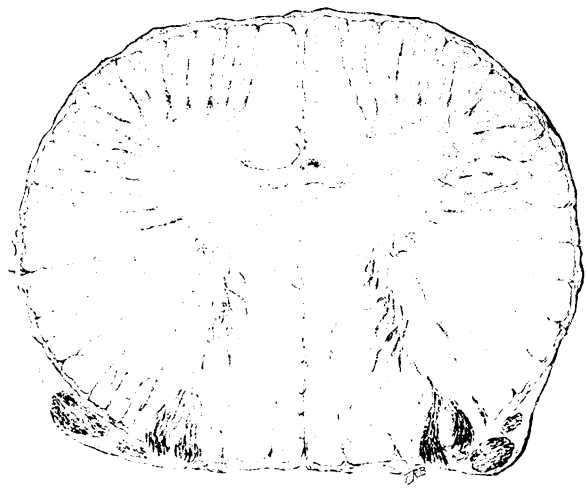

Fig. 70.—Secondary descending degeneration. When a lesion is produced in the brain the nerve fibers below the lesion degenerate and it is this which causes the paralysis. This figure shows the area of degenerated fibers in the spinal cord after a hemorrhage into the internal capsule. (Delafield and Prudden.)

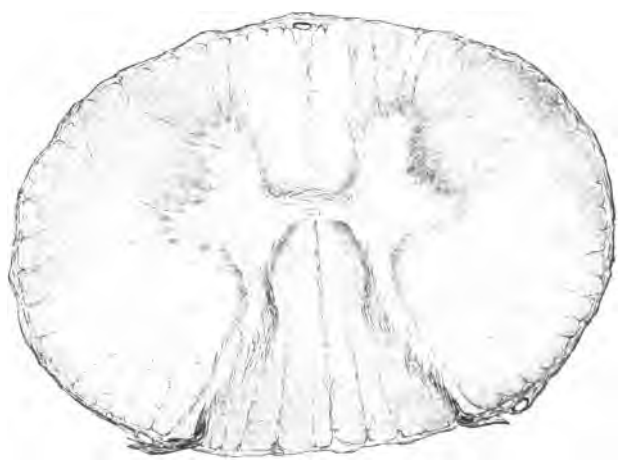

Fig. 71.—Amyotrophic lateral sclerosis. Sometimes all of the motor fibers of the spinal cord degenerate and lead to a progressively developing muscular paralysis. This figure illustrates the appearances of the spinal cord under such conditions. The pale areas are the degenerated ones. (Delafield and Prudden.)

upon the sort of influence which acts upon the system as a whole or upon any part of it.

The cells of which the nervous system is composed are perpetual cells in the sense that in the course of de-

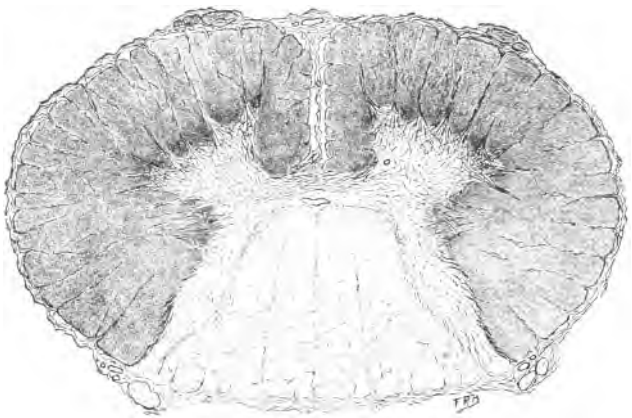

Fig. 72.—In tabes dorsalis (locomotor ataxia) it is the fibers in certain sensory (ascending) nerve tracts which degenerate. The appearances are shown in this figure. (Delafield and Prudden.)

velopment they have lost the power of reproduction. They are therefore incapable of regeneration and so when a cell or a group of cells have undergone necrosis they are completely lost to the organism, and their place

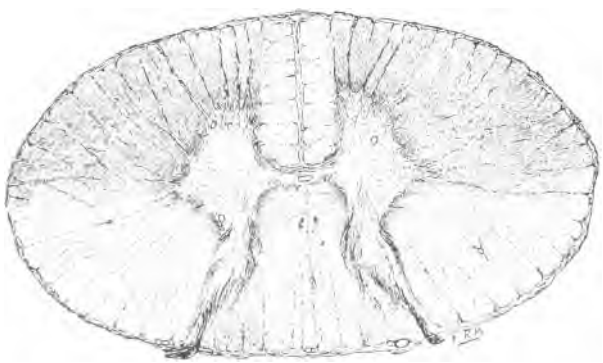

Fig. 73. When both ascending (sensory) and descending (motor) tracts are affected, the appearances in the spinal cord are a composite of those shown in Figs. 94 and 95. This figure illustrates this. (Delafield and Prudden.)

is taken by an overgrowth of glia cells, which, although they are of the same embryonic origin as the nerve cells, have preserved the power of growth and reproduction. Gliosis in the nervous system is the analogue of fibrosis in other organs.

Lesions of the nervous system may be divided into those which involve inhibition, loss, or intensification of the power of receiving impulses, of transmitting impulses (afferently or efferently), or of making associations.

1. Disturbances of the receiving and afferent transmitting mechanism (sensory).
   - Anesthesias
   - Paresthesias
   - Hyperesthesias
   - Ataxias (?)

2. Disturbances of the efferent transmitting mechanism (motor).
   - Paralyses
   - Tonic contractions (tetanic)
   - Clonic contractions
   - Ataxias and choreas (?)

3. Disturbances of the associative mechanism.
   Mental dissociation and abnormal associations.

Hallucinations	Amnesias	Hysterias
Amentia	Aboulia	
Dementia	Delusions	

4. General disturbances of the nervous system.
   1. Intoxications
      - Delirium
      - Coma
      - Convulsions
   2. Defective development
      - Idiocy
      - Imbecility
      - "Mental debility"

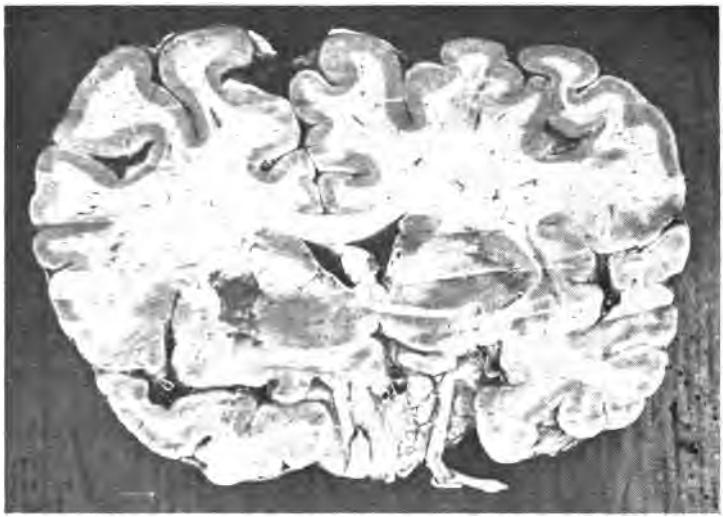

Fig. 74.—Section of a brain showing an area of softening resulting from a brain hemorrhage (apoplexy) in the thalamus and the internal capsule. Through the internal capsule the motor fibers to the muscles of the body pass. Destruction of these fibers lead to paralysis on the opposite side of the body. If the hemorrhage is on the left side the paralysis will be on the right.

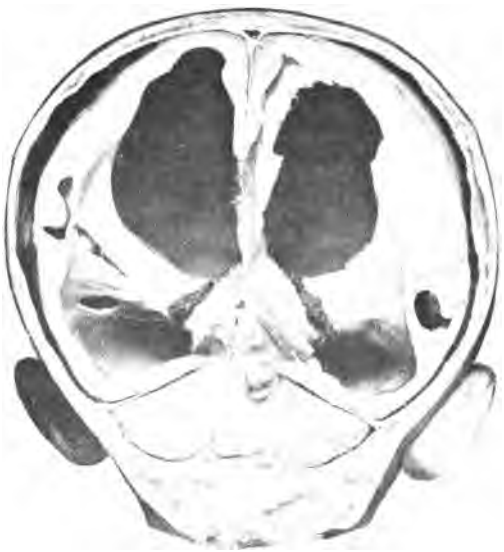

Fig. 75.—Coronal section through the cranium and brain of a case of chronic hydrocephalus, showing extreme distension of the lateral ventricles. (From the Pathological Museum, University of Sheffield.) (Beattie and Dickson.)

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CHAPTER XIV.

THE HEMOPOIETIC SYSTEM.

This system is composed of the lymph glands, spleen and bone marrow, and is named hemopoietic because of the fact that one of the functions of each of these organs is the production of the cells of the circulating blood, of the adult organism. As a matter of fact, the blood cell producing function is more closely associated with the bone marrow, and perhaps, under certain conditions, with the hemolymph glands. The spleen and lymph nodes are, on the other hand, of value rather as filters than as producers of cells. The hemolymph glands stand midway between lymph nodes and bone marrow. The general structure of all these organs is much the same, so that there is some reason to conclude that there is something common in their functions, a conclusion that seems to be justified in experience with clinical cases such as myelogenous leukemia, in which the whole system is, as a rule, changed.

The bone marrow is the chief blood cell producing tissue and, like other tissues, undergoes hyperplastic and retrograde changes. In certain types of disease, as in aplastic anemia, it seems to be completely fatigued so that it no longer produces. In less severe cases, as in the usual pernicious anemia, and the leukemias, it produces activity. There is evidence that in anemia from any cause the bone marrow increases in activity more or less in proportion to the circulatory losses.

The spleen, though it is a producer of cells, seems to be rather more important as a reduction plant when broken down cells, especially senile red cells, are filtered

out of the blood stream and prepared for re-using in the body. It is perhaps because of its reduction function that it may play a part in the neutralization of toxins which come to it bound to the cellular proteins. When the spleen is removed its functions are apparently assumed by the bone marrow and lymph glands. Evidence is accumulating that it is more commonly the seat of infections than was formerly supposed.

The lymph glands are of two indistinct orders: one, the ordinary lymph nodes, and, second, the hemolymph glands. Their importance resides in their filtration activities which are similar in some respects to those of the spleen, but which are devoted to the periphery of the body and with the lymphatic fluids rather than with the blood. Their especial value seems to be in combatting infections, during which they filter out and hold infectious organisms. They also furnish, especially under such conditions as exist in lymphatic leukemia, and in certain infections, small mononuclear cells (lymphocytes) to the blood.

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CHAPTER XV.

THE SUPPORTING AND LOCOMOTORY SYSTEM.

This system includes the bones, joints, muscles, tendons, and ligaments. The bones are of importance because they give rigidity to the body; the joints, because

Fig. 76. A case of rickets

they allow of a certain degree of flexibility; the muscles, because of their contractility, make motion possible; the tendons and ligaments preserve the positions of the

bones, and determine the amount and direction of movement at the joints.

The structure and composition of bone accounts for

Fig. 77. -A case of rickets.

its rigidity, and therefore variations in structure and composition will modify the normal rigidity.

Physical causes—

Trauma (fractures).

Metabolic causes—

Hyperplasias (tumors).
Atrophy (halisteresis, osteomalacea).
Inflammation (osteomyelitis).

Fig. 78.—A case of rickets.

Necrosis (metallic poisons).
Metaplasia (osteitis deformans).

The joints depend for their function upon the synovial membranes, and upon the ligaments and tendons, and so,

variations in structure and composition of these tissues will modify the effectiveness of a joint.

Physical causes—

Trauma (dislocations).

Metabolic causes—

Inflammations (arthritis).

Toxic arthritis (gout).

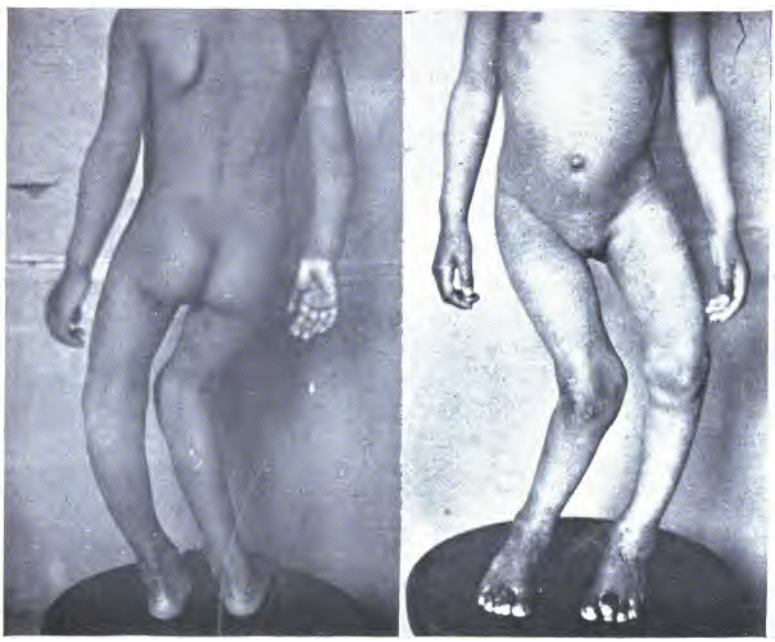

Fig. 79.—A case of rickets.

Lesions of nervous system (?).

Metaphasia (arthritis deformans) (?).

The functions of the tendons and ligaments depend upon their tensile strength and this upon their structure. Therefore variations in the structures of these tissues will modify their function.

Physical causes—

Trauma (rupture, strain, sprain).

Metabolic causes—

Inflammations (tendinitis; tenosynovitis).

The muscles determine the movements of the body, and movement is the expression of contractility. Variations in contractility of the muscles will modify in greater or less degree the movements of the body.

Physical causes—

Trauma (rupture).

Fig. [illegible] Showing extreme case of [illegible].

Metabolic causes—

Inflammation (myositis).

Atrophy.

Necrosis.

Intoxications (fatigue, anemia).

Tumors.

Lesions of nervous system (paralyses, spasms).

Fig. 81.—Extreme rickety deformities of the femur and the tibia. Note the flattening of the shafts of the deformed bones. (Edinburgh University Anatomical Museum. Catalogue No. OS.D.i.8.) (Beattie and Dickson.)

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